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The Influence of Fatigue on Health and Longevity

Syphilis and Industry

Trinitrotoluene as an Industrial Poison

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## PHYSIOLOGICAL EFFECTS OF AUTOMOBILE EXHAUST GAS AND STANDARDS OF VENTILATION FOR BRIEF EXPOSURES*


YANDELL HENDERSON, HOWARD W. HAGGARD, MERWYN C. TEAGUE, ALEXANDER L. PRINCE, AND RUTH M. WUNDERLICH


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### INTRODUCTION

THE increasing use of the gasoline engine in a widening diversity of fields has brought with it corresponding problems concerning the influence of exhaust gases upon the health not only of the men in immediate charge of the machines but of the general public as well. Reports upon a number of these problems have already been published by the United States Bureau of Mines, but, for the most part, recent studies have dealt particularly with the use of traction engines and the vitiation of the air in coal mines, and the determination of standards for the allowable vitiation requisite for safety.

The plan to construct tunnels under the Hudson River between New York and Jersey City for the use principally of motor vehicles has raised several problems which have previously, however, never been extensively investigated. Whereas the conditions in coal mines and about gas producer plants apply only to healthy men, the conditions which will prevail in the tunnel under the Hudson River will affect the general public. Not only healthy adults but children and even invalids on their way to hospitals will be transported through it, and at some time it may be necessary for soldiers to march through. The amount of traffic is likely to be large, even from the beginning, and is likely to increase in a few years to the maximum capacity of the roadway. The total amount of exhaust gas discharged from passenger cars and trucks will therefore be considerable. The distance between


* An abbreviation of the report to the Chief Engineer of the New York State Bridge and Tunnel Commission and the New Jersey Interstate Bridge and Tunnel Commission. The investigations were carried out under the Bureau of Mines at the Physiological Laboratory of Yale University. The full reports on both the engineering and the physiological aspects of this problem will be published in the report of the Chief Engineer of the Commissions and by the Bureau of Mines. Published here by permission of the Director of the U. S. Bureau of Mines and of the Chief Engineer of the New York State Bridge and Tunnel Commission and the New Jersey Interstate Bridge and Tunnel Commission. Received for publication Feb. 24, 1921.

the ventilating shafts at the pier heads on the two sides of the river will be somewhat more than 3,300 feet — a distance greater than in any existing tunnel used by motor vehicles — and the total length of the tunnel about 8,500 feet between portals. The ventilation must, therefore, be ample to prevent not only danger, but even slight discomfort, and must be managed in such a fashion as to avoid excessive wind velocities. The cost of installing ventilating fans will, in any case, be an appreciable item in the initial construction, and the maintenance of artificial ventilation during the operation of the tunnel is likely to be one of the largest single items of continuing expense.

Accordingly, the commissions of the states of New York and New Jersey through their Chief Engineer, Mr. Clifford M. Holland, contracted with the Bureau of Mines to undertake on their behalf the investigation of two problems: (1) the amount and character of the exhaust gas produced by various types and sizes of passenger cars and trucks; and (2) the nature of the toxic substances in exhaust gas, and their allowable concentration — that is, the extent to which the gas must be diluted with air to become practically harmless. The results of these two investigations will together afford the data upon which plans and designs for the ventilation of the tunnel may be intelligently based.

Problem 1 was placed in the immediate charge of Mr. A. C. Fieldner, supervising chemist of the Bureau of Mines at the Experiment Station of the Bureau at Pittsburgh. Problem 2, of which the results are here published, was assigned to Dr. Yandell Henderson, Professor of Physiology in Yale University and Consulting Physiologist of the Bureau of Mines. The work was carried out by him with a staff of physiologists and chemists employed by the Bureau for this purpose in the Physiological Laboratory at Yale University.

The investigations and formulations here presented are of a much wider scope than the mere solution of the problem raised by the Hudson tunnels. Vehicular tunnels are being very generally considered both as substitutes for bridges and as a means of decreasing distances and grades in highways in mountainous regions. Furthermore, the results of these investigations apply almost equally well to conditions in garages and fire rooms, to the air around gas producers, smelters and blast furnaces, to dwellings in which there is an escape of illuminating gas, and, in general, to all places where men are exposed to the gaseous products of incomplete combustion.

Prior to this investigation, the standards of allowable air vitiation with carbon monoxide have not been precisely defined. The investigations of Dr. J. S. Haldane, the eminent English authority, have dealt chiefly with questions of the safety of miners after mine explosions and fires, and his attention has, therefore, generally been directed to the amount of carbon monoxide which would incapacitate or seriously inconvenience a man, rather than to those amounts which are compatible with complete comfort and efficiency. For the London underground railways, however, he gave it as his opinion that a concentration of not more than one part of carbon monoxide in 10,000 of air was desirable. It is noteworthy, nevertheless, that he contemplated a possible period of exposure sufficient for the blood to approach equilibrium with this concentration in the air. The standard hereinafter proposed by the authors appears at first sight distinctly higher than that originally suggested by Dr. Haldane, but when the short time of exposure in the proposed vehicular tunnels is taken into consideration it will be seen that the figures reached by Dr. Haldane and by the authors for the amount of carbon monoxide absorbable without appreciable injury or discomfort are in quite close agreement.

It might appear that the ventilation of any closed space should be such as to furnish virtually as pure air as that of the city streets. In that case, this investigation would be unnecessary, and a standard of not more than one part of carbon monoxide in 10,000 of air might have been adopted. To have attempted, however, to ventilate long tunnels like those under the Hudson River, or any similar closed space, so that the air would be virtually free from carbon monoxide, would perhaps have proved scarcely practicable. It would certainly have been extremely expensive. The wind velocities necessary in moving such a volume of air would cause discomfort to passengers and might even prove prohibitive of traffic.

The standards here established will reduce the expense of ventilation greatly below that required to provide a carbon monoxide dilution of one to 10,000, not only in the Hudson tunnels, but in all similar future undertakings. These standards will, it is hoped, prove valuable both to hygienists interested in safeguarding the public health and to engineers engaged in the design of a wide variety of projects both above and below ground.

## I. Fundamental Considerations

Although carbon monoxide is the cause of more deaths than the total due to all other gases, apart from a single reaction it is a physiologically inert and non-poisonous substance. This reaction is its combination with hemoglobin, the red coloring matter and oxygen-carrying element of the blood. To whatever extent hemoglobin is so combined, it is rendered incapable of transporting oxygen from the lungs to the tissues and organs of the body, until the carbon monoxide is again displaced. It is highly probable that all of the results of inhalation of carbon monoxide are due directly or indirectly to oxygen deficiency. Even when other toxic substances are present — as in smoke, in fumes from explosives and in other incomplete combustions — carbon monoxide is usually the chief cause of injury or death. It acts wholly through asphyxia.

The body of an adult man of average weight contains enough hemoglobin to hold about 600 c.c. of oxygen. If completely saturated, it would hold the same amount of carbon monoxide, one molecule of carbon monoxide replacing one molecule of oxygen in the blood. The absorption of 6 c.c. of carbon monoxide from the lungs produces, then, 1 per cent. of saturation and abolishes 1 per cent. of the oxygen capacity.

The unit, in which various concentrations of carbon monoxide are commonly measured and expressed for purposes of ventilation, is one "part," or a certain number of "parts," of this gas mixed with 10,000 times as much air. A "part" is a hundredth of 1 per cent. of an atmosphere. A man at rest breathes about 8,000 c.c. of air per minute, of which about 6,000 c.c. reach his lungs, or 60 liters in ten minutes. Let us suppose that this air contains one part of carbon monoxide, or 6 c.c. in 60 liters, and that all of this 6 c.c. is absorbed. The blood would then become saturated at the rate of 1 per cent. every ten minutes per "part" of carbon monoxide in the air. Evidently the duration of exposure is a limiting factor in the amount absorbed, for one cannot absorb more than one inhales.

It appears that when a man begins breathing any low concentration of carbon monoxide mixed with air, absorption at very nearly this rate does occur, but only at first. Then the rate becomes slower. Even if the exposure is prolonged, carbon monoxide merely displaces oxygen from the blood up to a point of equilibrium depending upon the relative amounts, or mass actions, of carbon monoxide and oxygen in the air breathed and the intensity of the affinities of the two gases for

hemoglobin. If thereafter the pressure of oxygen is high enough and that of carbon monoxide is low, or absent as in pure air, oxygen can likewise displace carbon monoxide and thus completely restore the oxygen-carrying power of the hemoglobin. The blood is neither directly changed nor injured by the process.

Hemoglobin attracts carbon monoxide about 300 times as strongly as it does oxygen. Thus, if $T_{O_2}$ and $T_{CO}$ are the pressures of oxygen and carbon monoxide, and $Hb_{O_2}$ and $Hb_{CO}$ the amounts of oxyhemoglobin and carbon monoxide hemoglobin in the blood, the relations are expressed by the formula:

$$\frac{T_{O_2}}{T_{CO} \times 300} = \frac{Hb_{O_2}}{Hb_{CO}}, \text{ or}$$

$$\text{percentage } Hb_{CO} = \frac{T_{CO} \times 300}{T_{O_2} + (T_{CO} \times 300)};$$

or more specifically, if there are 1,500 parts of oxygen and 2 of carbon monoxide, the formula works out to:

$$\frac{2 \times 300}{1500 + (2 \times 300)} = 28.5 \text{ per cent. saturation with carbon monoxide.}$$

The air in the lungs contains about 1,500 parts of oxygen in 10,000. (It is actually somewhat less than 15 per cent. of oxygen. The affinity of hemoglobin for carbon monoxide may also be less, or more, than 300. We are here using round numbers merely to illustrate the principle without attempting mathematical precision.) We may calculate the blood equilibrium for any concentration of carbon monoxide in the air, and from such data we may obtain the carbon monoxide dissociation curve of the blood as shown in Figure 1. This curve indicates that, if air containing two parts of carbon monoxide in 10,000 is breathed for a time long enough to attain equilibrium, the blood should become about 28 per cent. saturated; with four parts, 44 per cent.; with six parts, 54 per cent.; and so on. In the curve it is to be seen that, for instance, the equilibrium value for ten parts of carbon monoxide in 10,000 of air is 66.6 per cent. saturation, which is a sufficient degree of saturation to render a man unconscious and totally helpless. If continued, the asphyxia might lead to serious permanent injury or even death.

The question of greatest practical importance is: How long a time would be required to attain this or any other definite percentage of saturation? In other words, what is the physiological law defining the rate of absorption of carbon monoxide into the blood? From the simple calculation, given previously, regarding the oxygen capacity of the body and the volume of air drawn into the lungs, it appears that a man breathing ten parts of carbon monoxide would inhale enough of the gas to become 66.6 per cent. saturated in 66.6 minutes. But, as already indicated, the more carbon monoxide the blood contains, the greater becomes the force with which this gas tends to diffuse out again into the air. The more nearly this tendency equals and counterbalances the pressure of the gaseous carbon monoxide in the lungs, the slower the absorption of more carbon monoxide becomes. Thus, to attain a condition of complete blood equilibrium many hours would be actually required; indeed, the time is indeterminate. Doubtless other factors also play a part in retarding and stopping absorption.

It appeared to us, however, that *a definite quantity for determination would be the time required for attainment of a percentage saturation of one-half the equilibrium values.* Thus, in an atmosphere containing two parts of carbon monoxide, for which the blood equilibrium is about 28 per cent., how long a time would be required for the blood to become 14 per cent. saturated? How long with four parts and an equilibrium value of 44, to attain 22 per cent. saturation; or with six parts and an equilibrium of 54, to reach 27 per cent.? The answer to

this question is the principal practical contribution to knowledge which we have to make — namely, that *the time for attainment of half equilibrium for persons sitting at rest and breathing concentrations of carbon monoxide up to seven parts is never considerably less than one hour*. This fact is, we believe, of fundamental importance for ventilation engineering. We have established it purely experimentally. It might, however, easily be correlated with the oxygen consumption and the carbon dioxide elimination, but we have not thought this to be of practical importance to the immediate object of this report. It does not, nor does it aim to, express what the average person does under the conditions, for many of our subjects fell much below this rate of absorption. The value of the rule is that it expresses the worst attainable, or, so to speak, the "maximum load."

We may here conveniently consider the question, often raised, of possible extreme individual susceptibility. Such susceptibility might conceivably arise (1) from anemia, that is, a subnormal amount of hemoglobin; (2) from an unusual avidity of the individual's hemoglobin for carbon monoxide; (3) from unusual susceptibility to the ill effects of oxygen deficiency; or (4) from a volume of breathing much above the ordinary. The first is unimportant practically inasmuch as anemics need not spend long periods in ill-ventilated garages, nor ride through tunnels on slow moving trucks. If, however, they are transported at the speed of a passenger car or an ambulance through a two-mile tunnel containing the average concentration of carbon monoxide here to be proposed, the time of exposure will be too brief to allow an absorption sufficient for any considerable ill effect. The second possibility has been investigated by us, but has not been found to occur. (Owing to their highly technical and space-consuming character, these studies are omitted here, but will appear in the full report.)

There is reason to believe that there are individual differences in the degree of the ill effects induced by considerable oxygen deficiency. Aviators and mountain climbers exhibit such differences, and in our more extreme tests headache has occurred in some persons at a somewhat lower percentage saturation of the blood than in others. We have, however, found no one who experienced this effect — the first sign of oxygen deficiency — under the conditions of the standards which we shall propose.

The volume of breathing is by far the most important element in the rate of absorption of carbon monoxide and, thus, in the individual variations in the ill effects of inhalation of this gas. In general, the expired air of a healthy man contains 4 or

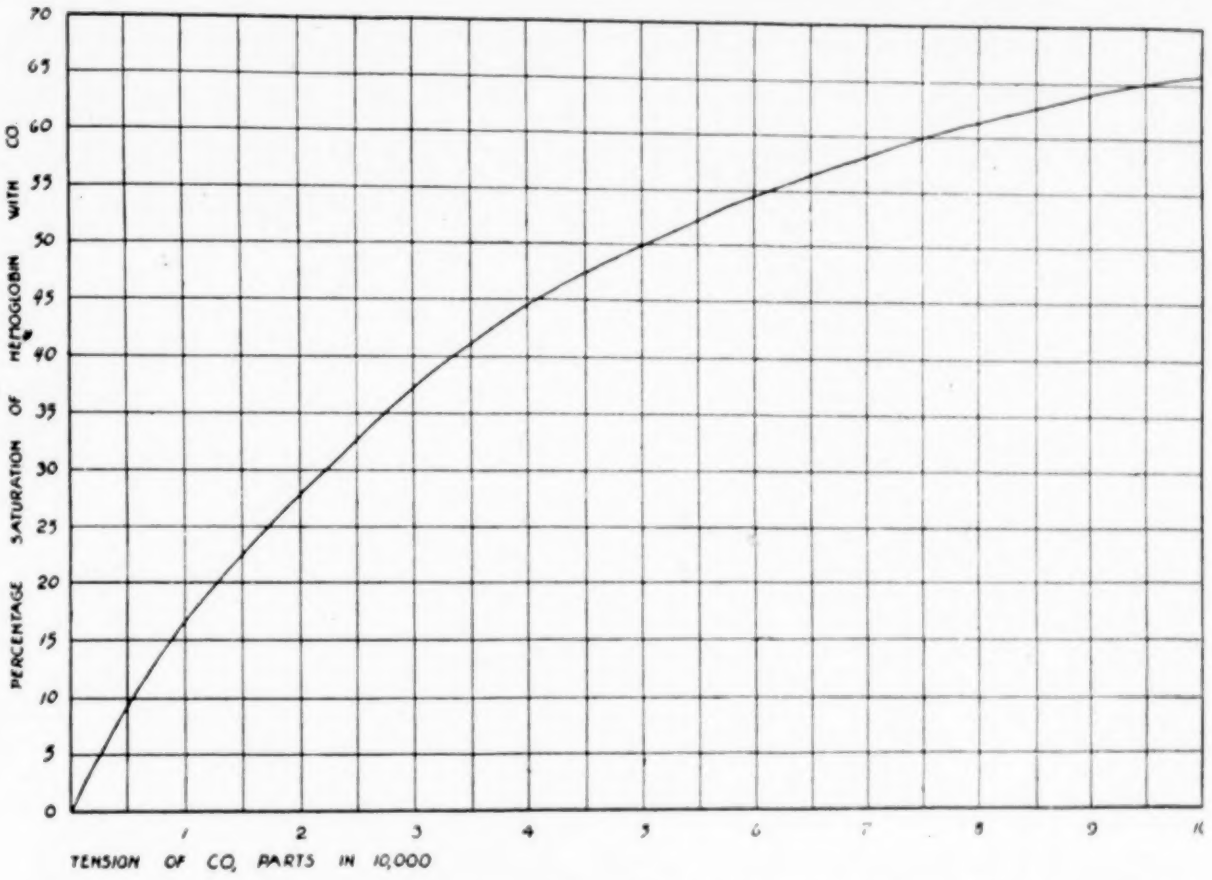


FIG. 1. — Final or equilibrium distribution of hemoglobin between carbon monoxide and oxygen when various low concentrations of carbon monoxide in air are inhaled for an indefinitely long time.

5 per cent. of an atmosphere less oxygen than the inspired air, and this percentage deficit is nearly the same during rest with a breathing of 8 liters and under physical exertion with a respiration several times as large. In other words, the volume of breathing is roughly proportional to the amount of the oxidation and energy liberation occurring in the body. In our observations, persons of vigorous physique and large breathing rates have absorbed carbon monoxide much more rapidly, as measured in percentage blood saturation, than those of more sedentary habit and delicate physique. As the standard which we shall propose is one adjusted to protect even the strong, it will therefore afford an extra safeguard to the weak and sick, who breathe little (except in febrile cases) and who would, accordingly, absorb carbon monoxide comparatively slowly. Only in the case of children, whose active vitality involves a relatively large food and oxygen consumption and a corresponding volume of breathing, will this rule probably not hold. But even for the most active child, a period of exposure of only ten or fifteen minutes to the concentration of carbon monoxide here approved will not be long enough for any considerable absorption of the gas.

The particular problem before us — that of a standard for the ventilation of the proposed vehicular tunnels under the Hudson River — may, therefore, be thus simply expressed: What percentage saturations of the blood with carbon monoxide cause appreciable discomfort in healthy men sitting at rest, and what percentage saturations do not? The answer to this question, the probable duration of exposure of passengers through the tunnel, and the law of carbon monoxide absorption as above stated, are the three considerations on which any sound standard must be based.

In view of the foregoing discussion it is, we trust, clear that standards of concentration, which will adequately protect men exposed for the greater part of an hour, will afford an enormous factor of safety for persons inhaling the vitiated air for only ten or fifteen minutes. We are informed by the engineers that all traffic through the tunnels will be in two distinct classes — namely, passenger cars, which will make the trip in ten or twelve minutes, and trucks which may take as long as thirty-five or forty minutes. The standards which we set ourselves to work out are such as will afford not only absolute safety but also complete freedom from any trace of discomfort for healthy and vigorous adults exposed for periods of forty-five to sixty minutes.

## II. Experiments on Men in Six Cubic Meter Chamber

The method of studying the effects of various concentrations of carbon monoxide upon which we have chiefly relied for establishing our standard is illustrated in Figure 2. It involves a chamber of 6.4 cubic meters, or 226 cubic feet, capacity, the walls and door of which are covered with galvanized sheet iron with soldered joints. The door is easily made gas-tight by placing long strips of broad (2-inch) adhesive plaster over the cracks along lintel, jambs, and sill. The chamber holds any concentration of gas for a day without appreciable loss from diffusion through undiscovered leaks. A small hole in the door, covered by a piece of adhesive plaster, allows the hand of the subject to be thrust outside for the withdrawal of blood.

Into this chamber are introduced measured amounts of pure carbon monoxide, made by dripping formic acid into strong sulphuric acid and distilling it by gentle heat into a large bottle filled with water, which the gas displaces. The concentration of gas desired in the chamber is obtained by running into the bottle 640 c.c. of water per

part of carbon monoxide desired, and thus displacing this volume of gas from the bottle through a tube into the chamber. An electric fan in the chamber insures immediate and complete mixing. In our experiments, two checks on the concentration of gas in the chamber were obtained: (1) by analysis of the carbon monoxide, before it was introduced, by means of a modified Orsat apparatus, and ignition with an electrically heated platinum spiral; and (2) by analysis of a mixed sample of the air from the chamber by the iodine pentoxide method, or by means of diluted blood. (For a description of these analytical methods, see bibliographical references 1, 2, 3.)

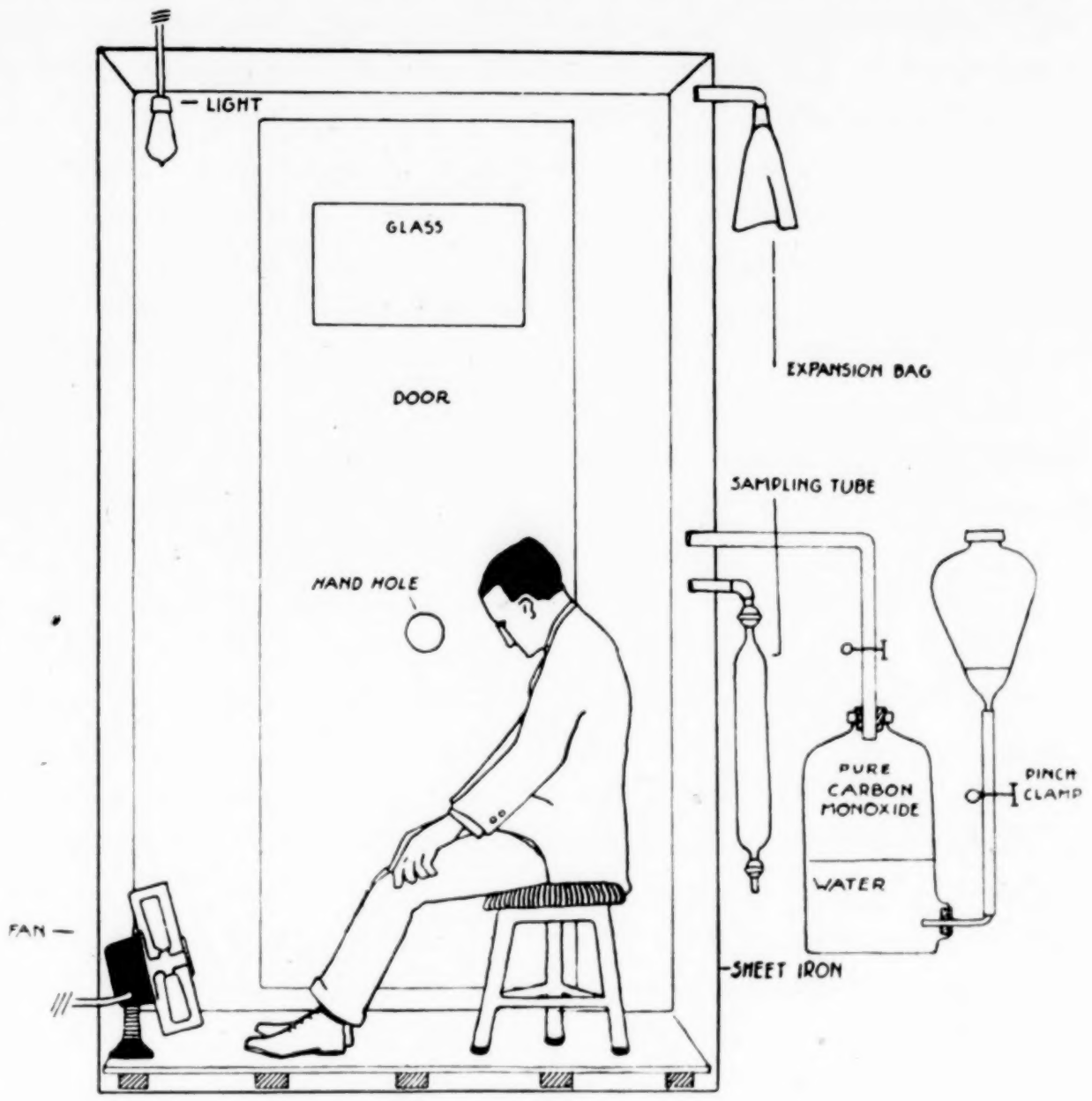


FIG. 2. — Six cubic meter chamber and apparatus for introducing measured amounts of carbon monoxide. This chamber consists of a wooden framework covered with sheet iron. It contains a chair, table, and electric fan. It can be hermetically sealed by applying long and broad strips of adhesive plaster over crevices between the door and the chamber walls. The hand hole in the door is also sealed by plaster. Through this hole the subject may thrust his hand when samples of blood are required for analysis.

With the diffusion fan running, measured quantities of water are introduced into the funnel. By opening the pinch clamps carbon monoxide is displaced from the bottle into the chamber. Samples of air for analysis may be withdrawn from the chamber by means of the sampling tube. A rubber bag allows for expansion or contraction of the chamber air with changes of temperature.

In this chamber, in turn, the members of the staff of this investigation and a few other persons spent periods of one hour after amounts of carbon monoxide from two to eight parts, and in one case ten parts, had been introduced. While the subjects sat and read most of the time, there were a sufficient number of acts—such as turning on the electric fan, standing up to look out of the window for a moment, opening and closing flasks to take air samples for later analysis, etc. — to correspond fairly well with the activity of the driver of a car. When we speak of the absorption of carbon monoxide by a person "sitting at rest," the condition must, therefore, be understood as only such moderate rest as this.

Blood, to the amount of twenty or thirty drops, was drawn from a finger before the subject entered the chamber; and 0.02 c.c. were drawn at the middle of the period and at the end, and usually once or twice during the next three hours. These blood samples were analyzed for carbon monoxide by the carmine method (3).

After the subject had been out of the chamber for a few minutes, the tension of carbon monoxide in his lungs, supposedly in equilibrium with the blood, was determined by breathing back and forth several times, during twenty to thirty seconds, into a rubber bag. Football or basket ball

"bladders" were used for this purpose. (A series of check determinations on four subjects showed that the maximum concentration of carbon monoxide from these bags was reached in five rebreathings during thirty seconds.) This air was then analyzed for carbon monoxide by the iodine pentoxide method, or by the blood carmine method. The subject's volume of resting breathing was determined either in or outside of the chamber by means of a mouthpiece, nose clip, double valves, and Douglas bag and gas meter; and the volume per minute was calculated.

In some experiments the respiration was increased by exercise, and the increase was measured and correlated with the correspondingly greater absorption of carbon monoxide. In these experiments the subjects did "stationary" walking or running in the chamber by lifting the feet and stamping. The exertion involved is considerable, but with care it can be kept quite uniform for half an hour at a time. The pulse was counted in the chamber, and before and after the test. The effects on the pulse and respiration of running up and down four flights of stairs, each 12 feet vertically, were also determined before and after the period in the chamber.

In a few cases the retinal fields were determined and plotted. With the degrees of anoxemia occurring in these experiments, however, the effects on vision in this respect were unimportant. The Romberg test, the ability to stand erect with eyes closed without wavering, was also used, and in some cases, after an hour in eight parts of carbon monoxide, it showed marked loss of equilibrium.

But of all signs and tests, both in the experiments in the small chamber here under discussion and in those that are to be described in the next section, the typical carbon monoxide, or oxygen deficiency, headache proved most definite and reliable. It is a distinctly localized pain, usually frontal, throbbing, intensified by lying down or by exertion. It is sometimes accompanied by more or less nausea, readily increasing to vomiting. The mind is not clear, except with an effort, and one's surroundings seem a little strange. The temper is easily upset, very much as in alcoholic intoxication, and the judgment is likely to be bad. There are wide variations in the degree of this headache, but in the experiments discussed in this section it was never extreme. On the border line it verged merely into slight lassitude. As a criterion of the effect of carbon monoxide, however, it is more distinct than any artificial test. Concentrations of gas too weak and periods of exposure too short to induce this sign in anyone may be considered entirely harmless.

From Table 1, in which the data of thirty-two experiments performed in this way on nine men and one woman are given, it appears that no one had an appreciable degree of headache after a period of one hour in the chamber with four parts of carbon monoxide or less, and that with six parts the effect, if any, was usually very slight. With eight parts there was decided discomfort for some hours, although not enough to interfere with efficient work in the laboratory or at the desk. After an hour in ten parts even an unusually resistant subject was rather miserable and averse to work for five or six hours, and could still recognize the effects after twelve hours. Examination of these data enables us to reach a working rule regarding the rate of absorption of carbon monoxide, for we find that up to and including concentrations of six parts of carbon monoxide in 10,000 of air the figures in column 3 of Table 1 do not exceed values of about one-half those for complete equilibrium given in Table 2 and drawn in Figure 1.

In other words, during one hour sitting at rest in such atmospheres, a man's blood never absorbs appreciably more than half

the amount of carbon monoxide which it would take up if he stayed in the atmosphere indefinitely. Inactive and small breathing persons absorb less. At concentrations of eight and ten parts of carbon monoxide the figures deviate slightly from this rule, but the rule of half saturation appears to be safe and convenient up to seven parts. It appears further that a man under exertion even more. These figures may be directly applied to conditions as they occur in regard to absorption of carbon monoxide. The estimation of the time required for half equilibrium must be shortened accordingly.

*Elimination of Carbon Monoxide.* — As regards the elimination of carbon monoxide after gassing, our data show that the proc-

TABLE 1. — PHYSIOLOGICAL OBSERVATIONS ON MEN IN SIX CUBIC METER GASSING CHAMBER [1]

| Number of Experiments | Concentration of CO in Air | Blood CO Percentage Saturation | Alveolar Air CO Parts in 10,000 | Pulse | | Symptoms |
|---|---|---|---|---|---|---|
| | | | | Normal | After Gassing | |
| | *Parts in 10,000* | *After One Hour* | *After One Hour* | | | |
| 2 | 2 | 11–12 | ..... | 70–80 | 70–76 | none |
| 3 | 3 | 13, 10, 14 | ..... | 72, 84, 74 | 72, 82, 74 | " |
| 11 | 4 | 22, 18, 17, 18, 14, 14, 20, 21 | 1.36, 1.33, 1.30 | 72, 74, 72, 76, 76, 70, 80 | 68, 76, 72, 80, 72, 74, 82 | " |
| 1 | 5 | ..... | 0.9 | ..... | ..... | " |
| 9 | 6 | 21, 16, 16, 25, 26, 17, 16, 18, 18 | 1.30, 1.26, 1.98, 1.20, 1.00, 1.24, 1.25, 2.30 | 72, 74, 80, 72, 74, 78 | 72, 74, 82, 72, 74 | none in seven cases, slight frontal headache in two cases |
| 4 | 8 | 32, 27.8, 34, 26 | 2.3, 1.4, 2.0 | 72, 76, 74 | 88, 80, 84 | decided headache four to eight hours |
| 1 | 9 | 34 | ..... | 76 | 80 | decided frontal headache; irritable for six hours; insomnia |
| 1 | 10 | 38 | ..... | 78 | 90 | throbbing frontal headache; irritable; at times Cheyne-Stokes' breathing |

[1] The figures in column 3 of the above table are seen to be never more than half the equilibrium values at concentrations of six parts, or less, in 10,000 of air. For equilibrium values see Table 2.

A number of experiments on the influence of exercise were also carried out in the chamber. When the volume of breathing was thus increased the rate of absorption of carbon monoxide was proportionally increased.

who exercises sufficiently to double the volume of breathing absorbs as much carbon monoxide in half an hour as he does at rest in one hour. We have found in other experiments, which need not be given here in detail, that when walking fast a man breathes about twice as much air as when sitting still and that when hurrying or doing rather heavy manual labor he breathes about three times as much, and ess is not complete until one or two hours, or even longer, after return to fresh air. Roughly, the rate of elimination is 30 to 50 per cent. per hour, depending doubtless on bodily activity and the volume of fresh air breathed. This evidence is summarized in Figure 3.

TABLE 2. — EQUILIBRIUM VALUES OBTAINABLE FROM FIGURE 1

| Parts of CO in Air | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|---|---|---|---|---|
| Percentage Saturation of Blood | 16.6 | 28.5 | 37.4 | 44.4 | 50.0 | 54.5 | 58.3 | 61.5 | 64.3 | 66.6 |

## III. Rate of Absorption of Carbon Monoxide and Standards of Allowable Vitiation of the Air

The essential practical results of the experiments in the 6 cubic meter chamber, and indeed of this entire investigation, are

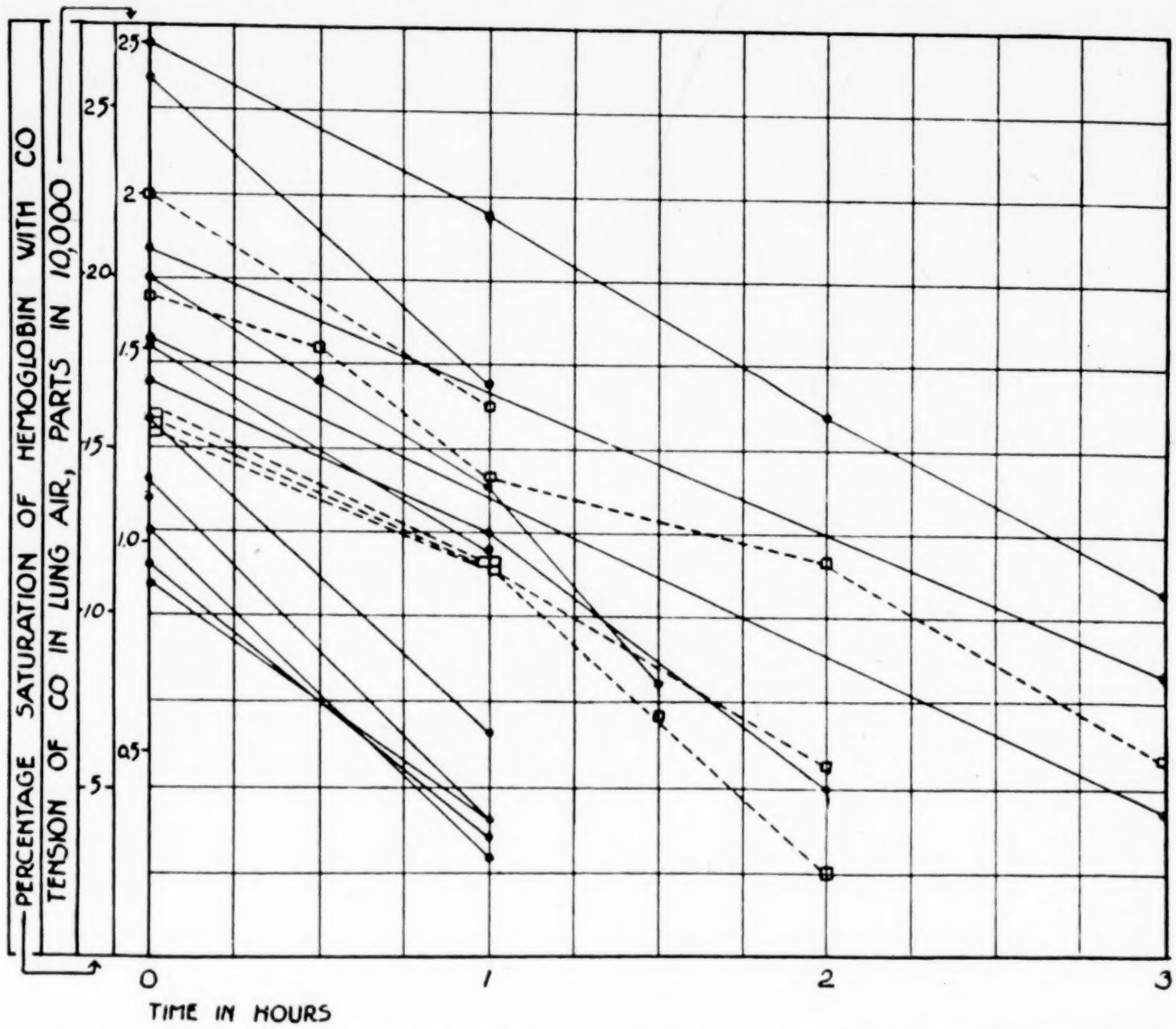


FIG. 3. — The rate of elimination of carbon monoxide after gassing. Solid lines are from analyses of blood, and dotted lines from analyses of pulmonary air.

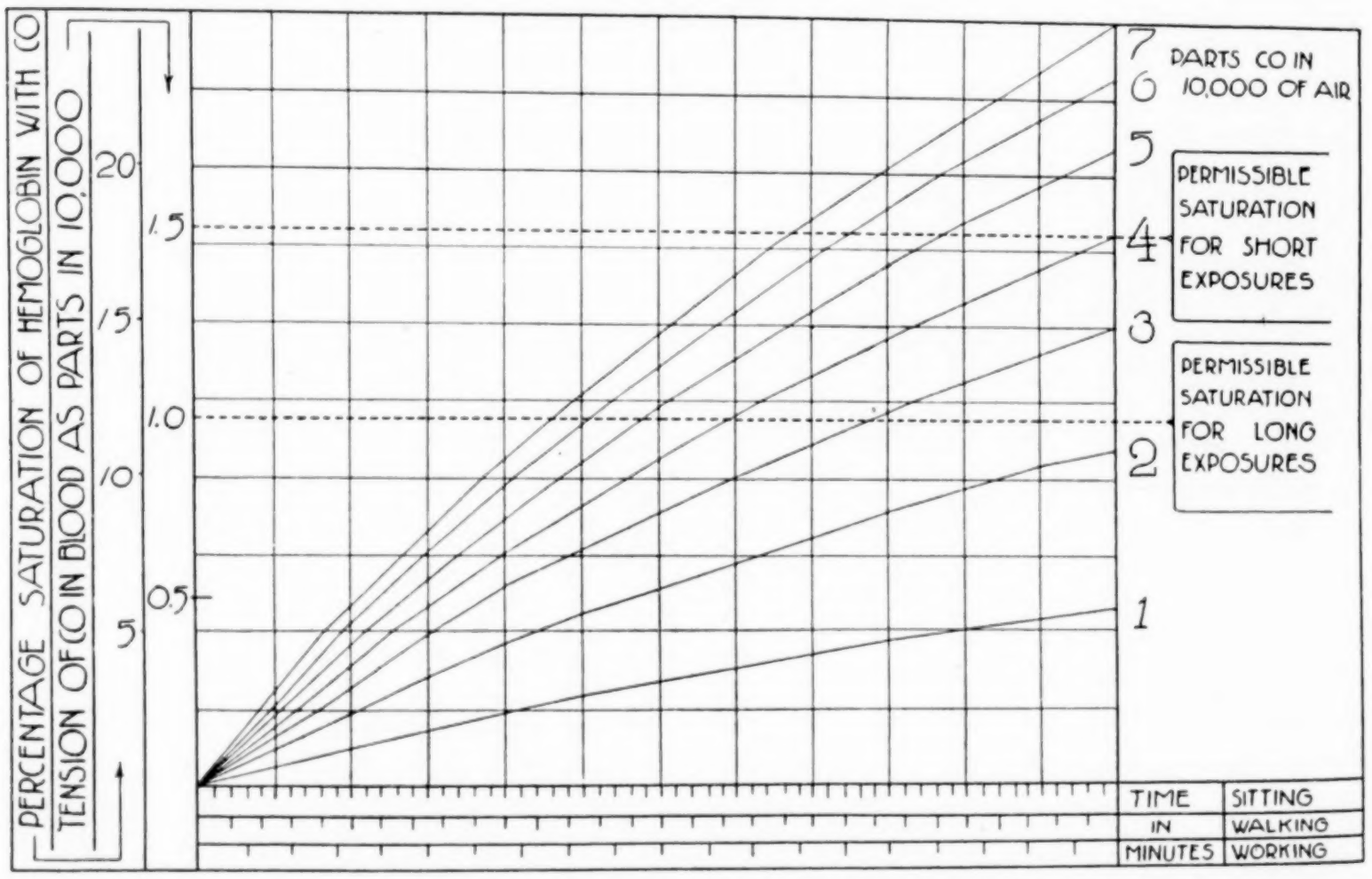


FIG. 4. — Curves showing rate of absorption of carbon monoxide by the blood in persons exposed to concentrations up to seven parts of carbon monoxide in 10,000 of air, for periods up to one hour, during rest (sitting), and for shorter periods of walking and working. For discussion see text.

summed up in Figure 4, which shows the rate at which carbon monoxide may be absorbed and the amounts at which physiological effects may occur. It is based on the data in Table 1, and is confirmed by the evidence obtained from experiments on a large number of people in the large gassing chamber — evidence which is to be presented in Section V. The curves are drawn to show the rate of absorption of carbon monoxide when air with various concentrations from one to seven parts of this gas in 10,000 is breathed. They express the absorption by the blood during one hour of one-half the amount of carbon monoxide that would be taken up after prolonged stay in each of these atmospheres.

One of the columns of figures at the left in this diagram expresses the percentage saturation attained by the blood; the other column shows the corresponding tension of carbon monoxide in the atmosphere in parts per 10,000 of air, with which the blood would be in gaseous equilibrium. In other words, the figures in column 2 indicate the amount of carbon monoxide that should be found in a pulmonary air sample, obtained by the method of rebreathing into a rubber bag, when the blood in the lungs contains these percentages of carbon monoxide. The three lines below the base line show respectively the (minimum) time required to reach these percentage saturations when the subject is at rest, when he is walking at a moderate pace and breathing a double volume of air, and when he is sufficiently active to breathe threefold, as a man at even moderate work may do. Horizontal dotted lines have been drawn at the levels of 12 and 18 per cent. blood saturation, corresponding to tensions of 1.0 and 1.5 parts per 10,000. The lower line indicates the amount of carbon monoxide which even after an exposure of several hours would not induce very disagreeable effects. The upper line expresses the level above which, in our experiments, slight discomfort and headache have sometimes resulted after an exposure of one hour.

This diagram has a very wide application. One may take off from the curves, by means of a pair of dividers, the quantities of carbon monoxide which may be absorbed by a person passing through any variety of concentrations of carbon monoxide, as may be the case in different parts of a tunnel. From the curves, one sees at a glance that if the tunnel is ventilated transversely so as to contain everywhere four parts of carbon monoxide in 10,000 — corresponding to 2,500 cubic feet of fresh air per minute per cubic foot of carbon monoxide produced by cars — a passage of three-quarters of an hour, the rate for slow trucks, would produce no appreciable discomfort. It is also evident when one plots the matter out, as has been done for the sake of illustration in Figures 5a, 5b, and 5c, that if the tunnel is ventilated longitudinally and the effluent air contains six parts of carbon monoxide, the physiological effect will be at least as good as with a uniform concentration of four parts in 10,000. In this case the ventilating fans need supply only 10,000 cubic feet of air for each 6 cubic feet of carbon monoxide thrown off by the cars in the tunnel, or 1,666 cubic feet of fresh air per minute per cubic foot of carbon monoxide. This is true if the air is forced in at one end and out at the other, and it is also true if the tunnel is ventilated in sections so that the air at some points contains only a trace of carbon monoxide and at others is contaminated progressively with from one to seven parts in 10,000 of air. This would be the case, for instance, if fresh air were driven in at the middle and ends of the tunnel and drawn out at the two intermediate points; *e. g.*, air shafts at the pier heads on each side of the Hudson River. This is illustrated in Figure 5d.

It is evident from this diagram that if at any point the concentration exceeds six

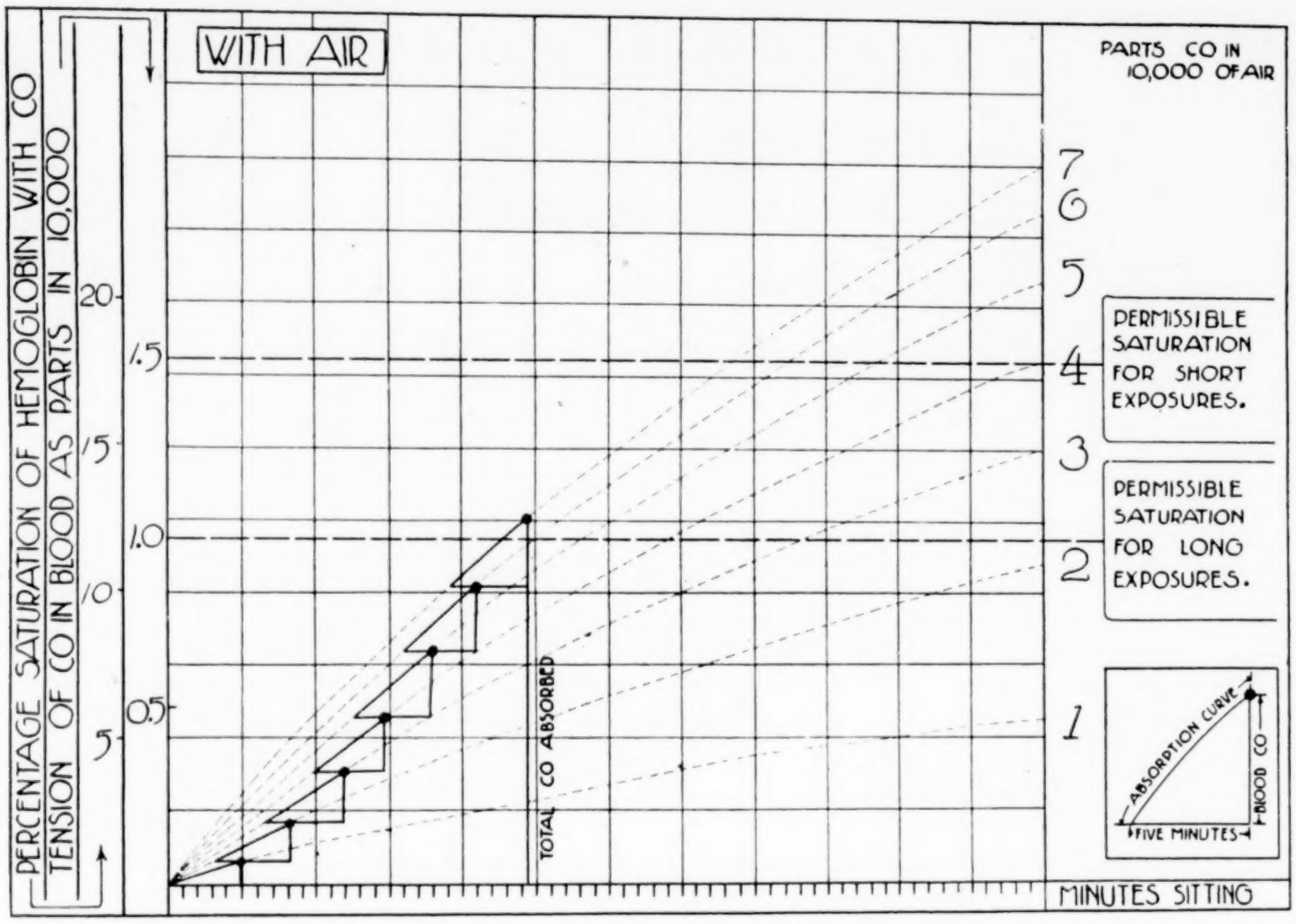


FIG. 5a. — Illustration of method for applying absorption curve data to specific conditions arising in a vehicular tunnel. Longitudinal ventilation. Subject in a sitting position travelling in direction of air current. Duration of passage through tunnel thirty-five minutes. The altitudes of the triangles express the increments of saturation of the subject's blood while passing through atmospheres increasing progressively in their carbon monoxide content. Effluent air = seven parts carbon monoxide in 10,000 of air.

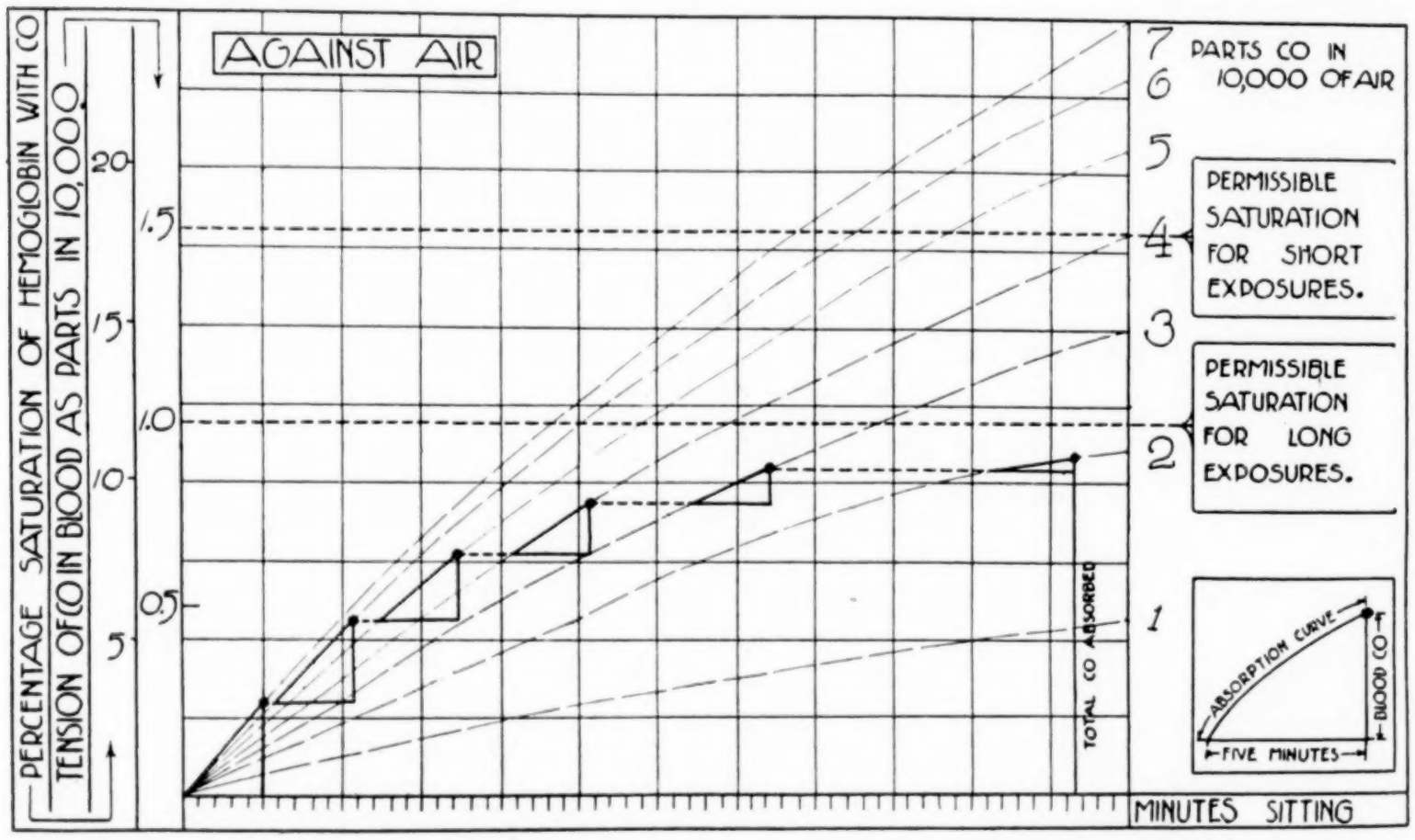


FIG. 5b. — Illustration of method for applying absorption curve data to specific conditions arising in a vehicular tunnel. Longitudinal ventilation. Subject travelling against air current. Duration of passage through tunnel thirty minutes. The altitudes of the triangles express the increments of saturation of the subject's blood while passing from effluent air containing seven parts of carbon monoxide in 10,000 through atmospheres decreasing progressively in their carbon monoxide content.

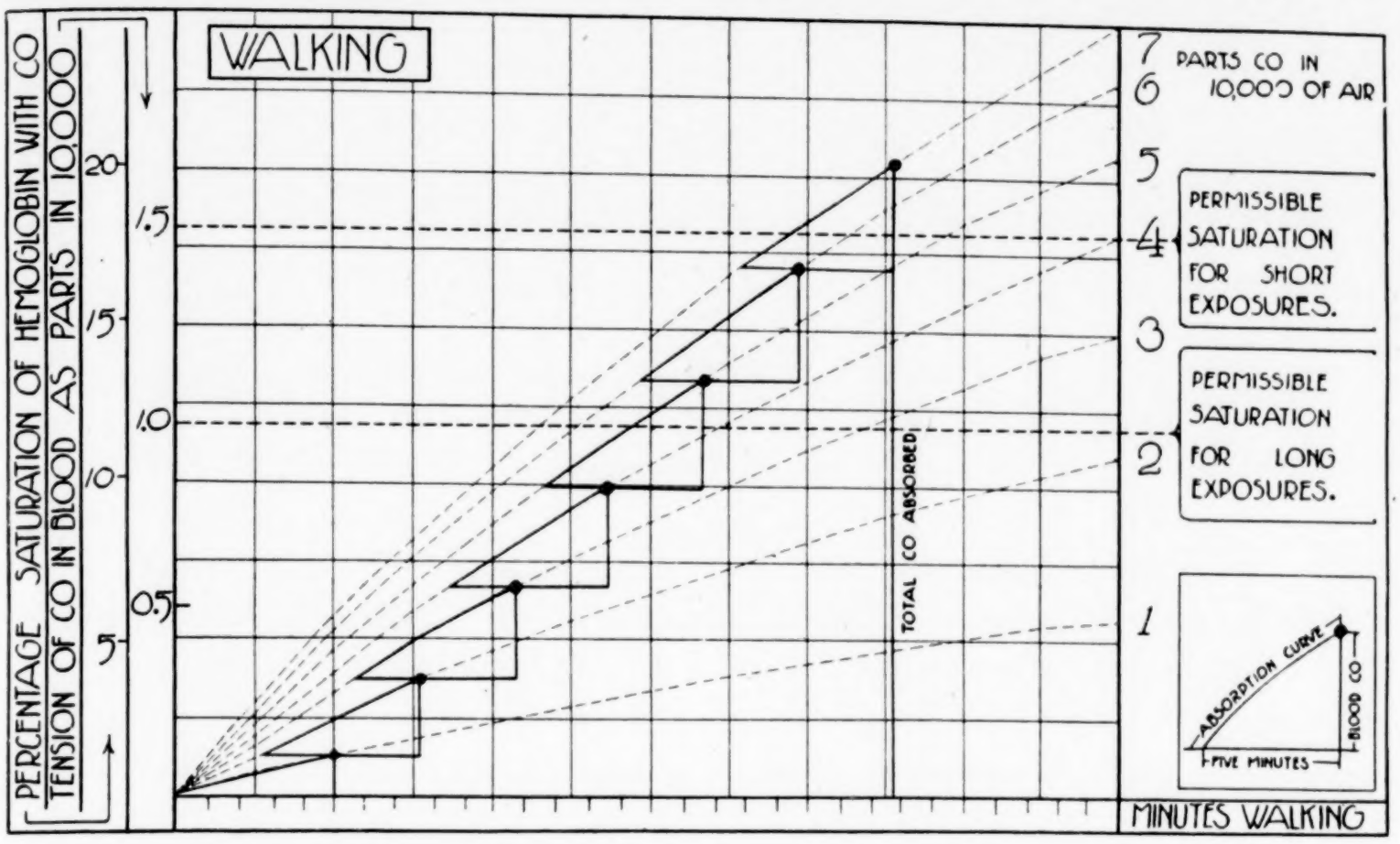


FIG. 5c. — Illustration of method for applying absorption curve data to specific conditions arising in a vehicular tunnel. Longitudinal ventilation. Subject walking in direction of air current. The altitudes of the triangles as under Figure 5a.

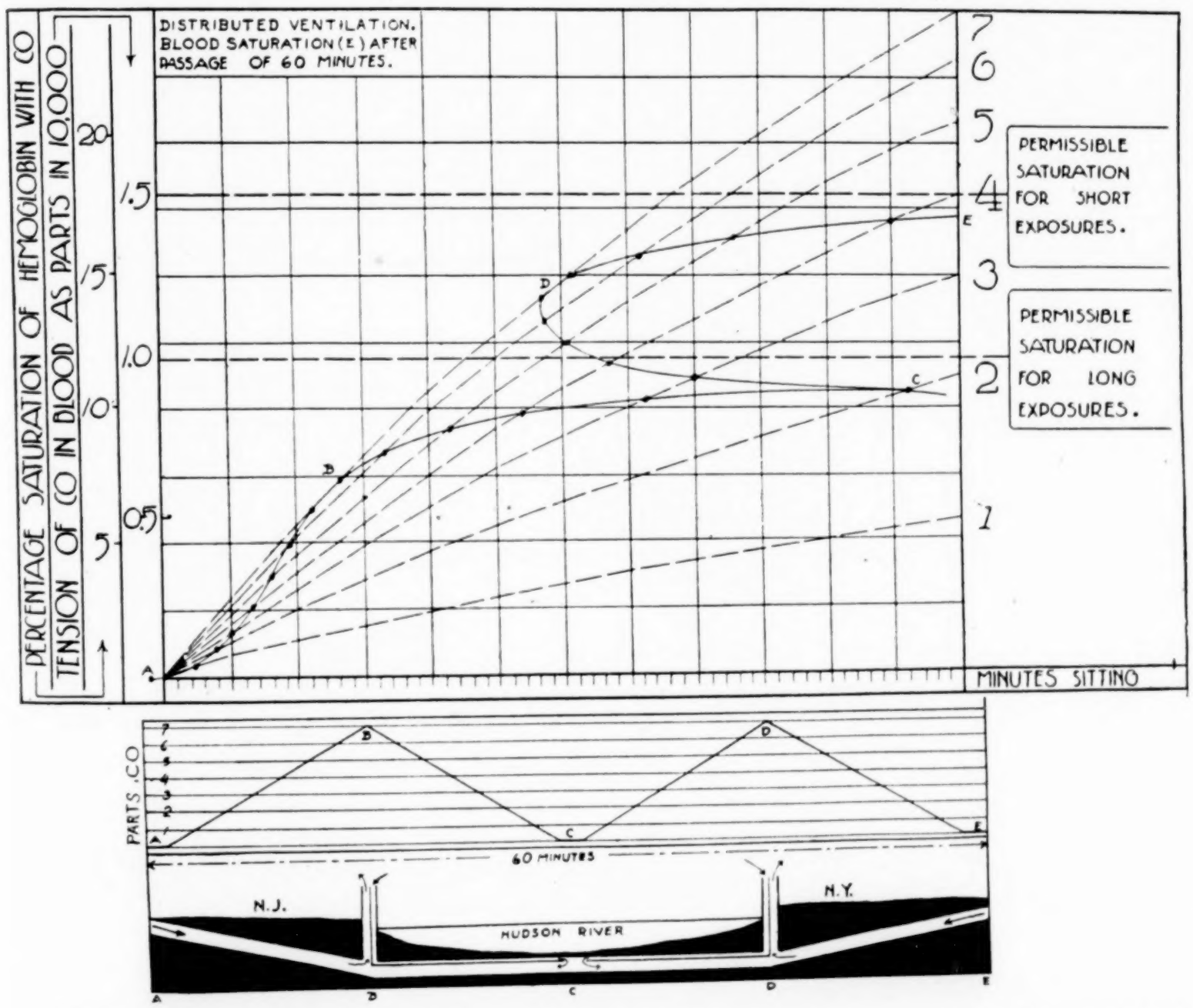


FIG. 5d. — Illustration of method for applying absorption curve data to specific conditions arising in a vehicular tunnel. Distributed ventilation. Subject in a sitting position travelling from A to E. Duration of passage through tunnel sixty minutes. The dots indicate the percentage saturation of the subject's blood at various stages of the passage. The letters A, B, C, D, and E indicate the percentage saturation of the blood when the corresponding points in the tunnel are passed.

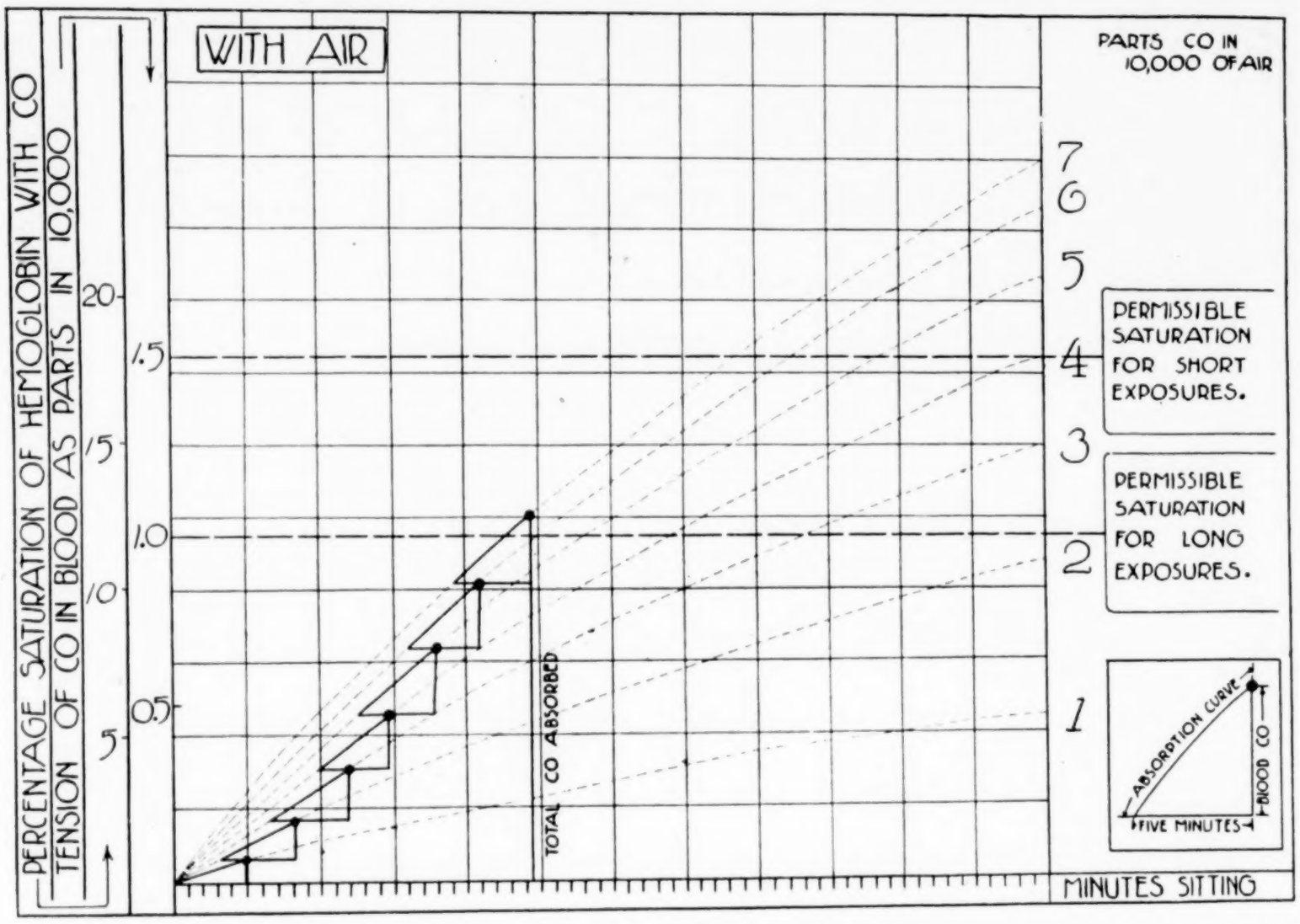


FIG. 5a. — Illustration of method for applying absorption curve data to specific conditions arising in a vehicular tunnel. Longitudinal ventilation. Subject in a sitting position travelling in direction of air current. Duration of passage through tunnel thirty-five minutes. The altitudes of the triangles express the increments of saturation of the subject's blood while passing through atmospheres increasing progressively in their carbon monoxide content. Effluent air = seven parts carbon monoxide in 10,000 of air.

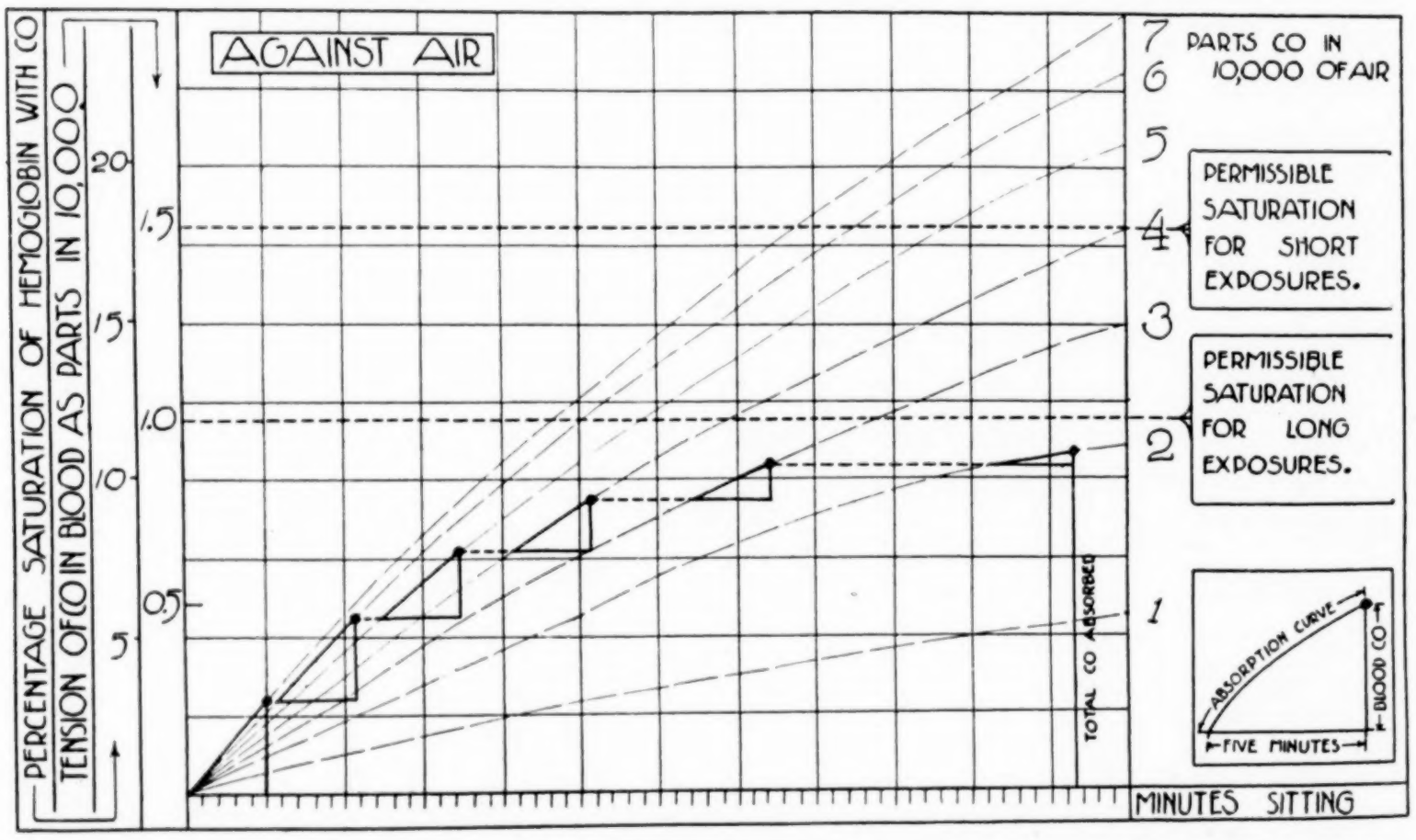


FIG. 5b. — Illustration of method for applying absorption curve data to specific conditions arising in a vehicular tunnel. Longitudinal ventilation. Subject travelling against air current. Duration of passage through tunnel thirty minutes. The altitudes of the triangles express the increments of saturation of the subject's blood while passing from effluent air containing seven parts of carbon monoxide in 10,000 through atmospheres decreasing progressively in their carbon monoxide content.

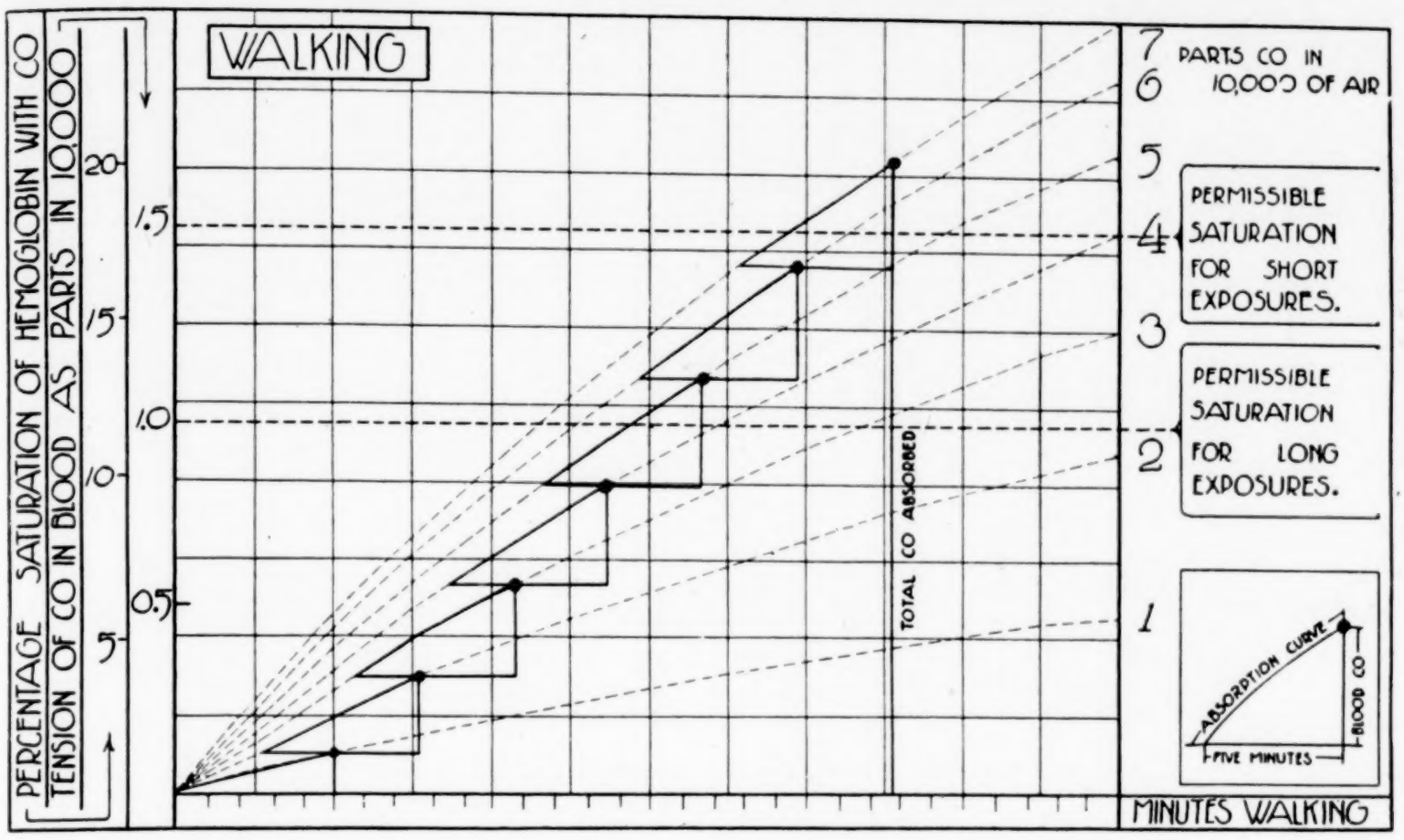


FIG. 5c. — Illustration of method for applying absorption curve data to specific conditions arising in a vehicular tunnel. Longitudinal ventilation. Subject walking in direction of air current. The altitudes of the triangles as under Figure 5a.

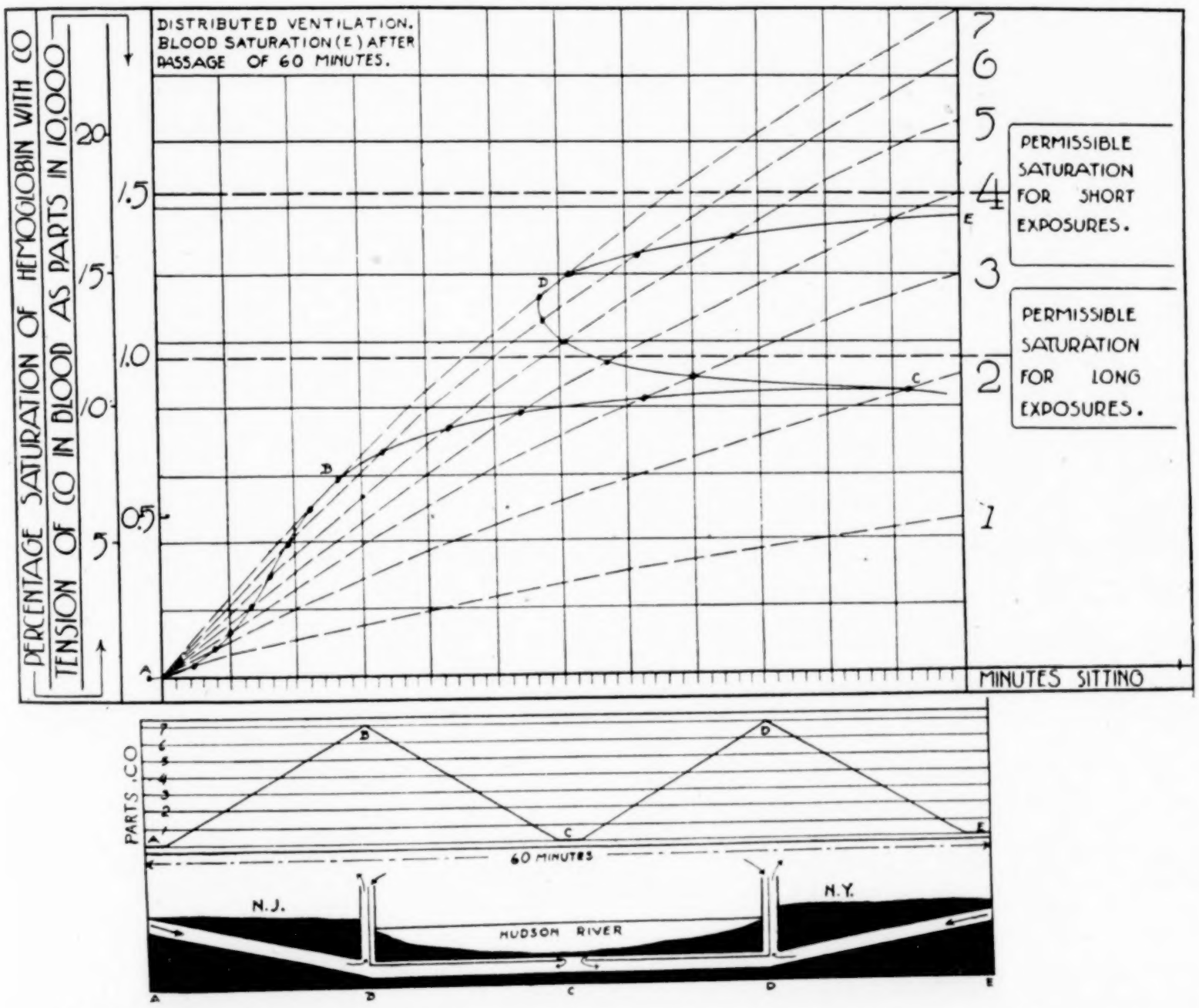


FIG. 5d. — Illustration of method for applying absorption curve data to specific conditions arising in a vehicular tunnel. Distributed ventilation. Subject in a sitting position travelling from A to E. Duration of passage through tunnel sixty minutes. The dots indicate the percentage saturation of the subject's blood at various stages of the passage. The letters A, B, C, D, and E indicate the percentage saturation of the blood when the corresponding points in the tunnel are passed.

parts of carbon monoxide in 10,000 of air, men doing hard work for even a short time will be unfavorably affected. On the other hand, the curves show that passengers in cars going through the tunnel in ten or fifteen minutes will absorb very little carbon monoxide — a factor of safety which is, we believe, sufficient to afford ample protection for children and invalids. The standard here proposed for exposures of forty-five minutes — four parts in 10,000 or its equivalent in an average of concentrations from zero up to six in 10,000 — affords, in the light of our experiments, not only complete safety but also an assurance of freedom from disagreeable effects. Risk of considerable discomfort would begin at eight to ten parts of carbon monoxide in 10,000 of air in periods of one hour during rest and for shorter periods during exertion. Actual danger would begin with concentrations not very much higher and periods not very much longer. The point should be emphasized, however, that we are dealing only with a standard of chemical purity of the air. Other features of tunnel ventilation as, for example, wind velocity, moisture, temperature, etc., are not included in the standard here defined, nor is comfort in these respects assured by it.

(*To be continued*)

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# THE INFLUENCE OF FATIGUE ON HEALTH AND LONGEVITY*

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THE final and most important test of the fatigue of a man's calling is to be found in the effect which it has on his health and longevity. Provided that he does not suffer more sickness than men in the healthiest trades, and shows no greater mortality, he has little ground for complaint even if his occupation is such as to induce a considerable degree of fatigue. Such fatigue must be within physiological limits, and so long as it does not exceed these limits and become pathological, it does him little or no harm.

Unfortunately it is a by no means easy problem to determine the influence of fatigue on sickness and mortality. We know that in some occupations, such as those of the potter, stone quarrier, and file maker, the abnormal sickness and mortality experienced are due largely to the inhalation of dust. In other occupations, such as those of lead and arsenic workers, they are due to the poisonous action of the substances handled; and in others, such as sorting wool and hides, they are due to bacterial infection. Again, we know that industrial workers who have spent all their lives in the crowded quarters of town dwellings have, as a rule, a poorer physique than those brought up in more healthy surroundings, and for this reason they may show a greater sickness and mortality, apart from any occupational effect. For instance, Dr. Arkle (1) measured the height and weight of the boys in the different grade schools at Liverpool, and he found that while boys of 14 years of age from the higher grade schools were 61.7 inches in height and weighed 94.5 pounds, those boys of the same age from the council schools, who were the sons of unemployed and casual laborers, were 6.5 inches less in height and 23.4 pounds less in weight. Boys of intermediate social status showed intermediate measurements.

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## Sickness Records

It is, nevertheless, of such importance for us to determine what effect, if any, fatigue may have on sickness and longevity that even a preliminary and imperfect attempt at its estimation is instructive. Such an attempt I have recently made in one of the heaviest of our industries, the iron and steel trade (2). Under the National Health Insurance Act the sickness of all industrial workers in Great Britain has been systematically recorded since 1913, and much of this material is in a form suitable for statistical treatment. Working in conjunction with Mr. E. A. Rusher, F.I.A., an actuary of long experience, I tabulated the sickness and mortality records of about 24,000 iron and steel workers for a six-year period, 1913–1918, and Mr. Rusher and his staff have worked up this material according to approved actuarial methods. My object was to separate the men into clearly defined occupational groups, the character of whose work was well known to me as the result of close observation. Among the steel workers, five clearly defined groups of skilled men were thereby obtained, while a certain number of other skilled men, whose numbers were too small to admit of their consideration as separate groups, had to be thrown into the general group of unskilled laborers and others.

The number of days of sickness per year suffered by these occupational groups are

recorded in Table 1. On an average they came to 6.5 working days per year, and in addition there was a small amount of time (estimated as 0.6 day) which is not compensated for under the Insurance Act, and which is not included in the recorded figures. The group of steel melters (on open hearth furnaces), teemers, and pitmen head the list, and show 23 per cent. more sickness than the average of all the workers combined. Next come the puddlers of wrought iron, with a 20 per cent. excess; then, the tinplate mill-men with a 12 per cent. excess; and then the rolling-mill men, with an 8 per cent. excess. All of these men work under trying conditions of high temperature, especially the first three groups mentioned, while the engine men and the general workers, who for the most part work under ordinary conditions of temperature, were found to show 8 or 9 per cent. *less* sickness than the average. At first sight, therefore, we seem to have a clear relationship between cause and effect, but an analysis of the time lost under the various categories of sickness does not altogether bear out the simplicity of the relationship. Sickness was classified under (*a*) rheumatism (acute and chronic), lumbago, myalgia, and neuritis; (*b*) pneumonia, bronchitis, influenza, pleurisy, catarrh, and sore throat (but not phthisis); (*c*) injuries incurred when following employment; (*d*) sickness due to other causes, and injuries incurred apart from employment.

It will be seen from Table 1 that the excess of sickness experienced by the puddlers was due entirely to rheumatism and respiratory diseases, probably resulting from the habits of the men. The puddlers generally work in couples, and they put in alternate periods of about twenty minutes of very strenuous work at puddling their molten iron, and of comparatively light work. They perspire freely during their heavy work, and as they sit about a good deal during their intermediate periods, usually in a draft, they render themselves very liable to chills. The tinplate millmen, whose work is on the whole as hot and heavy as that of the puddlers, show no excess of rheumatism and respiratory disease. This is due, I believe, to the fact that these men work continuously throughout their six or eight-hour shift. I kept groups of them under observation for several days, and I found that they seldom took rest pauses of more than four minutes'

TABLE 1. — DAYS OF SICKNESS PER YEAR EXPERIENCED BY STEEL WORKERS AGED 16 TO 70 (1913–1918)

| Occupation | Approximate Number of Workers | Days of Sickness per Year Due to | | | | | Percentage Variation from Average of All Workers Combined | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Rheumatism | Respiratory Diseases | Injuries | Other Causes | All Causes | Rheumatism | Respiratory Diseases | Injuries | Other Causes | All Causes |
| Steel melters, teemers, and pitmen | 1,740 | 1.3 | 2.2 | 1.2 | 3.3 | 8.0 | +44 | +10 | +71 | +14 | +23 |
| Puddlers | 970 | 1.6 | 2.7 | 0.7 | 2.8 | 7.8 | +78 | +35 | .. | −3 | +20 |
| Tinplate mill men | 2,090 | 0.9 | 2.1 | 0.8 | 3.5 | 7.3 | .. | +5 | +14 | +21 | +12 |
| Rolling-mill men, soaker men, hot-bank men | 2,470 | 0.9 | 2.0 | 0.9 | 3.2 | 7.0 | .. | .. | +29 | +10 | +8 |
| Engine men, crane men, locomotive men | 1,660 | 0.6 | 2.2 | 0.4 | 2.8 | 6.0 | −33 | +10 | −43 | −3 | −8 |
| All other workers (largely laborers) | 11,740 | 0.8 | 1.9 | 0.5 | 2.7 | 5.9 | −11 | −5 | −29 | −7 | −9 |
| All workers combined | 20,670 | 0.9 | 2.0 | 0.7 | 2.9 | 6.5 | .. | .. | .. | .. | .. |

duration, and never rested more than nine minutes (3).

It will be seen that most of the extra sickness suffered by the tinplate mill-men is due to "other causes," and it is possible that this is the result of fatigue, which lowers their resistance to disease in general. The steel melters show an excess of sickness from rheumatism and from respiratory diseases, as well as from "other causes," and this general excess definitely suggests a fatigue effect. The work done by the steel melters when fettling (*i. e.*, mending) the bottom of their furnaces is more strenuous and exhausting than any other kind of industrial labor with which I am acquainted. It obliges the men to approach to within a few feet of the partly open doors of the white hot furnace, and to push away the pools of molten steel with a kind of rake or "rabble." Subsequently the depressions in the bottom have to be filled up with dolomite or other material. This heavy work is very intermittent, and it lasts, on an average, only an hour or less per shift. After doing it the men not infrequently change their wet shirts. Also, unlike the puddlers, they are often provided with shelters into which they can retire, so there is some reason for thinking that their excess of rheumatism and respiratory disease may be due not only to chills arising from their work, but to lowered bodily resistance, the result of fatigue.

On separating the workers according to age groups, it was found that the older men, of 55 to 69 years of age, lost 6.3 times more time from rheumatism than the young men of 16 to 29. This great increase was specially observed in the men working at high temperatures, and the older steel melters and pitmen lost no less than 7.7 times more time than the young ones. On the other hand, the older engine men and "other workers" lost only 3 to 5 times more time from rheumatism than the young men in the same occupations. It is true that the total number of days lost by the older men in no case exceeded 3.1 days per year, but it is probable that the efficiency of the men would be lowered for weeks every year, rather than for days, in consequence of rheumatic pains.

TABLE 2. — DAYS OF SICKNESS PER YEAR AMONG BLAST FURNACE MEN BY AGE GROUPS

| Occupation | Days of Sickness per Year by Age Groups Due to | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Rheumatism | | | Respiratory Diseases | | | All Causes Combined | | |
| | 16–33 | 34–48 | 49–69 | 16–33 | 34–48 | 49–69 | 16–33 | 34–48 | 49–69 |
| Barrow fillers | 1.0 | 1.1 | 3.8 | 2.7 | 2.6 | 4.2 | 8.5 | 7.5 | 12.7 |
| Laborers and helpers | 1.3 | 1.0 | 4.0 | 2.3 | 2.6 | 4.9 | 6.6 | 7.8 | 15.9 |
| Other workers | 0.4 | 1.3 | 2.7 | 2.3 | 2.0 | 3.6 | 4.4 | 7.9 | 13.1 |
| All workers combined | 1.0 | 1.1 | 3.4 | 2.4 | 2.4 | 4.1 | 6.8 | 7.7 | 13.6 |

Data relating to blast furnace men are recorded in Table 2. They were obtained from a different "Approved Society" (working under the Insurance Act) from that of the steel workers, and they are classified in different age groups. They relate to 1,002 blast furnace men, and they show that men of 16 to 48 years of age experienced one to two days' more sickness per year than the steel workers, while men of 49 to 69 experienced about four days' more sickness. The excess of sickness was due partly to respiratory diseases, but especially to rheumatism. Thus, the men of 49 to 69 lost 3.4 days from this cause, while steel workers of the same age lost only 1.7 days, or half as much. It seems highly probable that this excess of sickness from rheumatism and respiratory disease

was due to exposure to the weather, for it was specially marked in the barrow fillers and the laborers, who are almost always working in the open without any kind of protection from the elements. It was less evident in the other and more protected group of men, which includes the keepers, molders, gas men, cleaners, engine men, and crane men.

## Mortality Records

It is extremely difficult to obtain adequate mortality records, for though very extensive records are collected and published at ten-year intervals by the Registrar General, they relate to such large occupational groups as to be of little value for our special purpose. For instance, the iron and steel workers whose sickness has just been discussed are placed with iron founders and with the makers of iron goods (such as stoves and bedsteads) in one comprehensive group, and no separation into individual occupations is possible. Accordingly, I had to fall back upon the mortality records of the steel workers already referred to, but data relating to 3,540 blast furnace men were obtained.

The total deaths recorded among the 20,670 steel workers in the six-year period under observation came to 1,023, and those among the blast furnace men, to 337. The mortality rates have been compared with those of all males (occupied and retired) in England and Wales, in the years 1910–1912, and the "expected" numbers of deaths recorded in Table 3 are calculated from the Registrar General's data (4). From the final columns of the table it will be seen that while 1,018 deaths were "expected" between the ages of 25 and 65, only 964 deaths were observed. In other words, the steel workers showed 5 per cent. less mortality than the general male population. This must not be taken to indicate that steel manufacture is a healthy occupation, for the group of "all males, occupied and retired," includes many weaklings who are unfit for any trade, or only fit for light work, while most steel workers have necessarily to be healthy men of good physique. Men in the healthiest occupations have a much lower mortality. The comparative mortality figure, which gives a death rate in which due allowance has been made for age distribution between the ages of 25 and 65, is 753 for the steel

TABLE 3. — TOTAL DEATHS AMONG STEEL WORKERS (1913–1918) COMPARED WITH THOSE AMONG ALL OCCUPIED AND RETIRED MALES (1910–1912) BETWEEN THE AGES OF 25 AND 65

| Occupation | Respiratory Diseases | | | Tuberculosis | | | All Causes Combined | | |
|---|---|---|---|---|---|---|---|---|---|
| | Actual Number | Number Expected | Percentage Variation from Number Expected | Actual Number | Number Expected | Percentage Variation from Number Expected | Actual Number | Number Expected | Percentage Variation from Number Expected |
| Steel melters, teemers and pitmen | 35 | 16.0 | +119 | 15 | 20.1 | −25 | 125 | 104.5 | +20 |
| Puddlers | 30 | 11.6 | +159 | 7 | 11.2 | −38 | 66 | 73.1 | −10 |
| Tinplate mill men | 22 | 14.8 | +49 | 7 | 21.0 | −67 | 69 | 99.3 | −31 |
| Rolling-mill men, soaker men, hot-bank men | 36 | 16.7 | +116 | 11 | 24.0 | −54 | 114 | 112.9 | +1 |
| Engine men, crane men, locomotive men | 22 | 13.0 | +69 | 10 | 17.3 | −42 | 77 | 86.5 | −11 |
| All other workers | 165 | 81.2 | +103 | 55 | 110.3 | −50 | 513 | 541.6 | −5 |
| All workers combined | 310 | 153.3 | +102 | 105 | 203.7 | −48 | 964 | 1,018 | −5 |

workers, as compared with 790 for all males, occupied and retired. In the healthiest occupations, such as gardening, the figure is 457. That of farmers and graziers is 495, while at the other end of the scale come potters with a mortality figure of 1,196, and stone getters and masons with one of 1,427.

Again, there can be no doubt that all the mortality figures recorded in Table 3 underestimate the death rate. In many trades, especially in the heavy occupations, there is a continual weeding out of some of the less vigorous men, who drift into the ranks of the casual and unemployed workers, and the removal of these weaker men lowers the death rate of those remaining in the trade. The records showed that about 1 per cent. per year of the skilled workers aged 54 or less disappeared, while 3 per cent. of the older men suffered the same fate. Among the "other workers" class the proportions were about twice as great. It follows, therefore, that it is impossible to gauge the effect of industrial work upon mortality with any approach to accuracy unless the history of all the workers can be traced after they have dropped out of their trade. Nevertheless, the data recorded are roughly comparable among themselves, and they show clearly that some occupations are more harmful than others. We see that the steel melters and pitmen head the list, and have a mortality 20 per cent. greater than that of all males, or 26 per cent. greater than the average of the whole group of steel workers investigated. This figure corresponds closely with the sickness figure, which was 23 per cent. above the average, and it suggests that the fatigue of the steel melters' work is responsible not only for more sickness, but for a loss of several years in the average expectation of life. It will be seen that the steel melters experienced more than twice the usual mortality from respiratory diseases, and, in fact, every one of the groups of men in the various occupations experienced a somewhat similar excess from this cause. From tuberculosis (almost always phthisis) the steel melters experienced about three-fourths the usual mortality, while the other groups of men experienced only one-third to two-thirds as much. This result was probably due in part to the fact that almost all the men were working in the open air or in sheds. Such exposure tends to reduce phthisis, though it may increase the risk of respiratory diseases in general. There can be no doubt, however, that many tuberculous workers drop out altogether from the strenuous work required in the iron and steel trade before death carries them off.

TABLE 4. — MORTALITY OF BLAST FURNACE MEN (1913–1918)

| Age Group | Percentage of Deaths per Year among | |
|---|---|---|
| | Blast Furnace Men | All Males |
| 16–33 | 0.8 | 0.4 |
| 34–48 | 1.3 | 0.9 |
| 49–58 | 2.7 | 2.0 |
| 59–69 | 5.8 | 4.4 |

The puddlers, who showed almost as much sickness as the steel melters, had a slightly lower mortality than the average, but their mortality from respiratory disease resembled their sickness from the same cause in showing a maximal value. The engine and crane men showed a smaller excess of deaths from respiratory disease than any other group except the tinplate mill men, presumably because they were not so much exposed to the weather or to high temperatures. The comparative immunity of the tinplate mill men from fatal respiratory disease is presumably due to their custom of working continuously during their shift, without any long rest pauses, and at the end of the shift going back promptly to their homes, which are usually situated in the neighborhood of the works.

The blast furnace men showed a considerably higher mortality even than the steel melters, as can be seen from Table 4, the data in which relate to the whole body of blast furnace men. These figures suggest that moderately heavy work, if carried out under ordinary temperature conditions but with exposure to all kinds of weather, is more fatal than very heavy work, carried out at high temperatures but with shelter from the elements.

## Conclusion

The data as a whole appear to indicate that in men of good physique the fatigue of heavy work has, as a rule, but little direct effect on sickness and longevity. It is probable that the excessively exhausting work of the steel melters forms an exception to this dictum, but it seems highly probable that the heavy work of the iron puddlers, of the tinplate mill men, and of the rolling-mill men has no injurious effect on health except indirectly, when it induces the men to sit about in damp clothes. The men may be working nearly to the limit of their strength, but the mere fact that they have to continue on the same class of work week after week and year after year must deter them from overstraining themselves, unless they do it unwittingly. At the time these observations were made, many of the steel melters, rolling-mill men and blast furnace men were on a twelve-hour day, while the puddlers were usually on an eleven-hour day. Since the spring of 1919 they have all gone on to an eight-hour day, so their labor is considerably lightened.

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# SYPHILIS AND INDUSTRY*

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THE objective of an occasional or periodic physical examination is to protect against future disease and accident — in other words, to extend life and promote efficiency. From the standpoint of the state, this objective may be more specifically described as the protection of the public health, by the recognition of communicable disease at the time of the examination, and the safeguarding of the future against dependency caused by depreciation of health or through injury which may result in permanent or transient, partial or total, mental or physical disability, and which may possibly call for the expenditure of public moneys for material relief.

For the individual, the periodic physical examination furnishes a means of protection against communicable disease in his fellow citizen, as well as a means by which defects that may contribute to his own health depreciation or liability to injury may be recognized. The employer's objective, on the other hand, is the protection of the community in which his industry is located, of the worker as an economic unit, and of the material and equipment of his plant, through the early recognition of those contributory factors that tend to cause health depreciation or accident occurrence.

Any single factor that is of considerable prevalence, easy to recognize, and relatively simple to eliminate, and that is, at the same time, a known detriment to community welfare, individual health, and industrial efficiency, deserves greater thought than has hitherto been given to *syphilis*. No medical argument is needed to prove that syphilis is communicable and that, in its active stage with open lesions, it is a menace to people working in close contact, with common tools or utensils. Nor is proof required that the late disabling manifestations of syphilis of the nervous system cause accidents and contribute to damage of property. It is evident, however, that attention still has to be called to cardiac, nephritic, digestive, and other "diseases" as possible symptomatic indications of an underlying syphilis, often overlooked in the course of the usual routine examination.

Any short cut, if not practicable, is of no advantage, and a routine Wassermann test as a short cut undeniably has its impracticalities. It is relatively expensive. It hurts a little to have some one "stick a needle" into one's arm. It prolongs the examination. Its mere mention still brings forth much of the old stigma of "venereal" disease. Moreover, it requires careful interpretation of reports and often frequent repetitions. But none of these nor any other of its impracticalities is insuperable, so why not go around the obstacle instead of standing by and saying it cannot be done without a short cut through. As a matter of fact, the shortest way to the objective of recognizing syphilis is to be found in the longer procedure of the ordinary physical examination. Greater specializing in parts of the routine examination for certain occupations makes for easier recognition of special defects. Therefore, the more value there is attached to examinations designed to detect such defects, the more important becomes the recognition of syphilis.

The most primitive routine examination for employment calls for an "inspection" of the applicant, which necessitates, at least, looking at the individual. If the inspector looks while the person is walking, his gait may suggest locomotor ataxia. His eyes, also, by such signs as irregular,

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unequal pupils, etc., may be of significance. Moreover, while conversing with the applicant, defective hearing may be detected, as may also such voice defects as monotony, harshness, or low pitch. Cervical glands may be palpated or an epitrochlear gland felt without actually doing more than a simple inspection requires. These danger signals, noticed during a very rapid inspection, call for further examination for the detection of additional signs that may lead to a diagnosis of "suspected" syphilis.

The average routine examination which calls for a simple history of past illness, an inspection of the head and neck, listening to the heart and lungs, and palpation of the inguinal region for hernia, markedly enlarges the opportunity for finding signs and symptoms of syphilis. Not only the obvious signals of abnormal gait, irregular and unequal pupils, defective hearing and voice abnormality may be detected, but also, with practically no consumption of time, the observant examiner may note the reaction of the pupils to light and accommodation; the presence of interstitial glossitis, leukoplakia, and Hutchinson's teeth; glandular enlargements (particularly epitrochlear nodes); scars (circular, pigmented, depressed, attached to underlying bone); and cardiac conditions (especially aortic valve disease). The finding of any *one* of these signs calls for further examination; the presence of *two* indicates the necessity for a Wassermann test for confirmation of suspected syphilis.

Where nursing and clerical help are available for such work as the taking of the history, temperature, height, weight, eye tests, and hearing and voice tests, a complete physical examination can be made by the medical examiner in ten minutes or less if his routine procedure is thoroughly systematized. With the nurse making the eye observations for pupillary irregularity, inequality, and reaction to light and accommodation, the examiner's observation of the applicant's head, nose, and throat may detect interstitial glossitis, Hutchinson's teeth, leukoplakia, ulcers or scars of the nasal septum, cervical adenitis, suggestive scars on the forehead, angles of the mouth, and alae of the nose, etc. While the examination of the heart and lungs is being made, the examiner may exercise his powers of observation to take cognizance of the skin of the chest, back, and arms for rash and scars not evidently due to injury or acne, at the same time that his ears tell him whether or not any aortic valve condition exists. Likewise, his examination of the abdomen enables him to "double up" and look for the same signs while palpating. A hard, palpable liver is one more signal. In examining for hernia, the telltale syphilitic inguinal glands may be found, as well as the testicle that has become harder and larger than usual. There are, too, other possibilities in the examination of the genitalia. Similar skin inspection of the lower extremity takes no time, and but a moment is required for an investigation of the knee jerks.

In making these observations, only a moment or two is added to the examination time, and, as syphilis is an important consideration for industry, it will be suspected in a high percentage of cases. In most cases showing more than one of the above-mentioned signs, the suspicion will be confirmed by a further examination, including the Wassermann test. If the desideratum is a simple examination consuming the least possible amount of time, it is possible to set down a series of syphilis signs that will guide the average examiner in culling out those individuals who require more detailed consideration and from whom it is desirable to procure blood for a Wassermann test.*

* When, as a result of any type or form of physical examination, evidence suggestive of lues of the nervous system is ascertained, it should be a routine procedure to do a lumbar puncture with a serologic examination of the cerebrospinal fluid.

In summary, it may be said that if any one, or any combination, of the following easily observable signals can be found, further examination for the detection of syphilis is necessary: ataxic gait; mental slowness; defective hearing; voice defects; pupils, irregular, unequal, or reacting abnormally to light and accommodation; enlargement of the lymph glands, especially of the epitrochlear nodes; interstitial glossitis; leukoplakia; Hutchinson's teeth; scars not obviously due to injury; cardiac conditions; and altered reflexes, especially knee jerk.

The industrial physician is probably justified in taking the view that a routine Wassermann is not possible at the present time, but he is not justified in overlooking the easily observable signs and symptoms that will promote the health of the employee and protect the employer from responsibility for preventable accidents.

# TRINITROTOLUENE AS AN INDUSTRIAL POISON*

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IN the summer of 1918, the National Research Council undertook an inquiry into the occurrence of industrial poisoning in munition works, and as one feature of this study they assigned to six typical T.N.T. plants medical students who had been trained in laboratory methods and in making clinical observations, in order to have them collect important data on the spot. The work was carried on in co-operation with the U. S. Department of Labor, the Public Health Service, and the War Department. The plants which were selected manufactured trinitrotoluene, or purified the crude, or loaded shell with pure trinitrotoluene or with the mixture of ammonium nitrate and T.N.T., known as amatol. Six students spent from one to two months at the plants assigned them, making observations on selected groups of the men and women employed there. Although the results of their studies, coming as they did in the fall of 1918, could not be put to practical use because of the closing down of these plants when the armistice was signed, it seems worth while to publish them because compounds very similar to trinitrotoluene are coming into increasing use in American industry. It is not likely that any other derivative of the benzene ring will ever be used on so gigantic a scale as was T.N.T. during the war, and all the information that was gathered during that great human experiment should be made known because of its probable application to the less well known compounds which are used in the manufacture of dyes and drugs.

At the time this study was made we had been able to learn a good deal about T.N.T. poisoning and its prevention from the British, but several points were still a matter of controversy, and it was to these that we devoted special attention. A study of industrial poisoning in the manufacture of explosives, which had been published by the Bureau of Labor Statistics in 1917, had shown that in American plants, as in the British, all varieties of T.N.T. poisoning were to be found from the so-called "minor T.N.T. sickness" to fatal toxic jaundice (1). The first death from the latter in England was reported in February, 1915, and the first death in this country came to light just about a year later (2).

T.N.T. is made by the nitration of toluene either by a continuous or by an interrupted process. There is little danger of exposure to poison for the workmen engaged in nitration, but the subsequent separation and purification of crude T.N.T. was, in this country, attended with very decided risk of poisoning — a risk actually as great as in shell loading. This was apparently not true in England, for there the great majority of cases of poisoning developed in the "filling," or, as we call them, loading plants. Thus, there were in Great Britain, in 1916 and 1917, 370 cases of toxic jaundice with ninety-six deaths, but only sixteen of the cases and two of the deaths were reported from the manufacturing plants (3). The nitration and purification of T.N.T., so prolific a source of T.N.T. poisoning in American munition plants, was evidently carried on under far greater precautions in England than here.

Commercial T.N.T. is mainly composed of the symmetrical isomer, a hard, crystalline powder, pinkish yellow if fairly pure, melting and subliming at 82° C. The im-

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purities present in crude T.N.T. and to a certain extent in the purified T.N.T. consist in insignificant quantities of the two other isomers and a varying percentage of mononitrotoluene and dinitrotoluene, and also nitrated methanes. Early in the war the question arose whether T.N.T. poisoning was caused by the pure substance or by one of the above impurities, and the suggestion was made that cyanosis and minor T.N.T. sickness might be caused by T.N.T. but that some other substances might be responsible for toxic jaundice and aplastic anemia. The British (4) came to the conclusion that pure T.N.T. was capable of setting up all these varieties of poisoning, while the Germans (5) concluded from their experience that toxic jaundice appeared only when impure T.N.T. was handled, and that tetranitromethane was probably the compound responsible for it. With this, the French (6) experience harmonized.

All the early efforts in Great Britain to prevent T.N.T. poisoning were directed against contamination of the air by fumes and vapors. Moore's experiments (4) threw doubt on this mode of entrance for T.N.T. and showed the importance of skin absorption. Indeed, he went so far as to declare that there was no need of carrying off fumes from melting pots, and that dust caused poisoning only because it fell on the skin and on work benches and objects which the workpeople had to handle. The other British authorities took a more conservative stand on this question, and the Home Office experts insisted on the prevention of fumes (3), but the overwhelming importance of the skin as a portal of entry for T.N.T. was generally admitted.

A great help in solving the questions of absorption, elimination, the relative danger of different kinds of work and of different mixtures containing T.N.T. was found in the so-called Webster test for the urine (4). This is a method of detecting in the urine a reduction product of T.N.T., dinitrohydroxylamino-toluene, and as it is a color reaction varying from a pale pink to a deep purplish pink according to the quantity of this reduction product present, there was no difficulty in standardizing it and thus bringing the observations of the different students into harmony.

The students assigned to the nitrating, purifying, and shell-loading plants were asked to make observations on problems of a thoroughly practical character, for although the United States had been in the war for more than a year the government had not yet formulated a sanitary code for the control of the explosives industry, and all attempts to do so met with opposition — an opposition which, it was felt, might be overcome if the managers of these plants were confronted with a body of facts gathered from American sources. The following questions were assigned to the students:

1. Can T.N.T. poisoning occur as the result of breathing fumes or dust, without skin contact?
2. Is susceptibility to poisoning influenced by race, sex, age, climate?
3. How long an exposure is necessary before T.N.T. can be detected in the body?
4. How long does it take to get rid of the T.N.T. that has been absorbed?
5. Which is more poisonous, crude T.N.T. or the pure; unmixed T.N.T. or amatol?
6. What are the earliest symptoms of T.N.T. poisoning?
7. What is the practical value of the Webster reaction?
8. Is there any change in blood or urine which can be depended on to give warning of danger?

Of the 402 workers who were examined in the six plants, only thirty-six were women. The conditions under which these people worked varied so much that some description of the plants will be necessary to account for the different results ob-

tained by the students. Plants 1 and 2 were assigned to Miss Alice Hall, a third year student at Rush Medical College. They were situated not far apart in northeastern New Jersey, in hot, shadeless country where the August heat of the summer of 1918 was at times excessively trying. Methods of work differed somewhat in the two plants, but they were both unusually neglected and unclean. The floors and benches, especially in one of the pouring rooms, were covered with drippings of molten T.N.T., the rooms were crowded and poorly ventilated, and both fumes and dust were allowed to escape into the air. The washing facilities were very inadequate, and, as they were not conveniently situated and time was not allowed for the men to bathe, they were not much used. Even the men who were cleanly in their habits found it very hard to keep clean, and naturally the labor turnover was very great and the force was for the most part recruited from the lowest class of labor. No instructions were given the workmen, and in neither plant did the physicians have anything to do with shop sanitation. Their duties were confined to holding office hours at stated times when men who fell sick and had confidence in the plant doctor could seek him out and ask for care. They did nothing to prevent sickness and not very much in the way of treatment, for if they thought a man likely to develop a serious case of poisoning, they promptly discharged him, for the protection of the company.

Miss Hall saw more cases of severe poisoning than did any of the other students, but she was hampered in her study of these cases because there was no hospital where they could be closely observed and because her notes of a case were usually brought to an abrupt end by the man's discharge or by his quitting of his own accord. She was never able to follow a case over a long period as could some of the other students.

In Plant 3, also in northeastern New Jersey, shell was loaded with amatol 50–50 and 80–20.* Miss Jewel Emery, laboratory technician from the Michael Reese Hospital, Chicago, spent a month there. It was a U. S. ordnance plant, new, clean, well constructed, and carefully managed, except that medical supervision was not thorough enough and there were no hospital facilities. The employees were of a better class than in Miss Hall's plants, but there was an unusually large proportion of young men among them.

Plant 4, which was in Virginia, was assigned to Richard TeLinde, a third year student in the University of Wisconsin Medical School. Shell was loaded in this plant with the two varieties of amatol. The plant was partly new, clean, large and well ventilated; partly old, rather crowded and dirty, and in some places very dusty. The men employed were negroes and southern whites, many of them from the North Carolina mountains, of poor physique and anemic. The medical care given at this plant was by far the best that we found anywhere, and included inspection of the men and women in their workrooms, the shifting of all suspicious cases from T.N.T. work to safe work, and the treatment of sick men in a well-equipped hospital. Mr. TeLinde was able to make observations on men for long periods and to follow a case of sickness to recovery, but he never saw as serious cases as did Miss Hall.

Plant 5 was in northern Wisconsin near Lake Superior. Here D.N.T. and T.N.T. were made, and purified and packed. The employees were decidedly superior to those employed in the other plants. Conditions were very good, there were ample facilities for washing, and medical care was good but insufficient, one physician with a part-time assistant not only having about 3,000 men under his care but also being responsible for the examination of all applicants

* Ammonium nitrate 50 per cent., T.N.T. 50 per cent., and ammonium nitrate 80 per cent., T.N.T. 20 per cent.

for employment. It was therefore impossible for the student at this plant to make as careful observations as were possible in Plant 4, especially as there was no hospital on the grounds. Norton Eversoll, a third year student in the University of Wisconsin Medical School, was assigned to this plant.

The work that was done in Plant 6 has already been described by Tracy Jackson Putnam and William Herman (7), the two Harvard Medical School students who spent a month there. Plant 6 was a purification, "finishing" plant, situated in the mountains of Pennsylvania. It was a fairly clean place except in two departments, and even those were not excessively bad, but the men were not given proper working clothes nor were the wash rooms adequate or comfortable. The medical care of sick men who applied for treatment was good, but there was no preventive work and no effort to discover cases of poisoning. Both negroes and whites were employed.

## Mode of Entrance of T.N.T.

It was impossible for us to obtain as clear evidence on the mode of entrance of T.N.T. as was gained by the British in their carefully regulated factories. No American plant was clean enough to make skin absorption even a rarity. Everybody employed in every department came in contact with T.N.T. dust and had his skin more or less covered with it. We could only make an effort to determine whether fumes and contact caused more poisoning than contact alone, and whether inhaling dust increased the incidence of poisoning. The reports from certain plants seemed to show that fumes and T.N.T.-laden steam decidedly increased the risk of poisoning. For instance, the graining, pelleting, and washing rooms of the purification plants, where fumes mixed with steam were more or less heavy, gave rise to many cases of sickness, especially in cold weather, when the doors were closed, and also in heavy, hot, summer weather.

According to Putnam and Herman, the procedure most dreaded in their purifying plant was cleaning out the bottoms of the great tanks in which crude T.N.T. had been boiled. The heat, moisture, and fumes in the tanks were overpowering and many men refused to enter them. Another piece of work which, according to the workmen, often caused deep cyanosis and fainting, was cleaning a room by volatilizing and melting with live steam the T.N.T. which had been spilled and splashed about. As for dust, it was found that pure, dry T.N.T. dust did not cause poisoning unless present in such quantities as to cover the skin of the workers. Pressing pure T.N.T. into detonator charges or demolition blocks seemed to be harmless work. On the other hand, small quantities of amatol (T.N.T.-ammonium nitrate) dust proved distinctly poisonous, although it contained only a small proportion of T.N.T.

A closer study of these findings led us to indorse the British view of the overwhelming importance of the skin as a portal of entry for T.N.T. because the same conditions that make respiratory absorption possible also increase skin absorption, and the greater toxicity of amatol as compared with pure T.N.T. depends on its greater absorbability. The instances given above of poisoning from steam and fumes can also be explained as due to the facilitation of skin absorption by heat and moisture. Grainers, pelleters and tank cleaners in purification works have their hands and forearms more deeply stained with T.N.T., even after a single day's work, than do men pressing charges at the end of several weeks' work. The dust of pure T.N.T. is not very readily absorbed by the skin. If one looks at the arms and hands of a man who is sifting or pressing dry unmixed T.N.T., one can see the powder covering the hairs of the skin, but unless the day is

hot enough to cause much perspiration this powder is dry and hardly stains the skin at all. In the graining and pelleting rooms not only is the T.N.T. which the men handle warm and wet, but the steam and fumes keep the skin moist all the time.

The same contrast was found by TeLinde between a drilling department where there was much amatol dust and a department in which pure T.N.T. was sifted. There was a great deal of sickness in the former department, and almost none in the latter. The amatol dust contained 50 per cent. of ammonium nitrate, and this, because of its hygroscopic nature, kept the skin of the workers moist. Tiny droplets of water could always be seen on the skin and hairs of the men's hands and arms, and on all the metallic surfaces in the room. Our experience in this country agreed with that of the British, who found that there was more sickness in connection with 80–20 amatol, containing only 20 per cent. T.N.T., than with pure T.N.T. We also found, as the British had, that oily substances favored the absorption of T.N.T. Two of the earliest American cases of toxic jaundice, one of them fatal, were in women exposed to very small quantities of amatol, but whose hands were smeared all the time with paraffin.

Although our observations showed that the skin is the chief channel of absorption for T.N.T., and that the prevention of poisoning means prevention of contact, still we were not convinced that T.N.T. fumes from grainers, washing tanks and melting kettles were harmless. Some of the students' case histories seemed to point quite clearly to fume poisoning, as, for instance, that of a new employee who was set to work on a fairly cool day in June stirring a kettle of molten T.N.T. which was poorly hooded. He became dizzy and faint, and went to the plant doctor who found him cyanosed, with weak and rapid pulse. He was suspended from work that day (Monday) but on the following Friday he was still feeling ill and his urine was still dark in color. Several students reported cases of men who, having once suffered from T.N.T. sickness, could go back to work with the substance, but if they were exposed to the fumes would suffer a return of the headache, dizziness, breathlessness and weakness with which they were familiar from their former experience. A very interesting report on this point was sent by Alice Hall. On two occasions she remained for two or three hours in the pouring room where the air was heavy with T.N.T. fumes, being careful not to touch anything during that time. After both these exposures she was able to get a positive Webster reaction. The superintendent of a department in one of the Navy arsenals, where depth charges and mines were loaded, told me that poisoning among his men was practically 100 per cent., not one of them having been able to work as long as three weeks without some symptoms of sickness. The fumes from pouring and from the cooling mines and shell were very heavy. He himself hardly ever came in actual contact with T.N.T., but he was frequently overcome with dizziness, headache and weakness if he had to stay in the fumes for many hours at a time. It is, of course, by no means certain that these fumes contain only T.N.T. and not some other substances equally toxic or more so.

## Influence of Race

The only students who had any opportunity to observe the difference between whites and negroes in their behavior toward T.N.T. were TeLinde in Virginia and Herman and Putnam in Pennsylvania. TeLinde was much impressed by the greater susceptibility of the white men. He did not find one case of T.N.T. sickness among the negroes. Negroes who were working alongside the whites handling

amatol sometimes gave a moderate Webster reaction, but their urines were normal in color, not dark, as were the urines of many of the white men in this department, nor did they complain of any symptoms of poisoning. In sifting pure T.N.T. by hand, only negroes were employed, and although the dust here was excessive, they gave a slight Webster reaction or a negative one. It is true that this dust was pure T.N.T. but that was also true of the dust in the drilling department in one of Alice Hall's plants, yet she found decided evidence of poisoning among the white men employed there and always got positive Webster reactions. On the other hand, Herman and Putnam, who were able to watch negroes and whites working together throughout the plant, found no difference in susceptibility of the two races. They examined thirty-seven whites and thirteen negroes. Among the latter were some who showed marked poisoning; indeed, the most typical case of T.N.T. poisoning that came under their observation was in a negro. They also found several negroes entirely unaffected after comparatively long periods of exposure.

It was apparent from TeLinde's report that the negroes in the Virginia plant were neither living nor working under the same conditions as the whites. They were, on the whole, more in the habit of taking baths than were the mountain whites employed there, and, living in their own cabins, they had a diet rich in fresh vegetables and fruit, while the white men ate in the company canteen where the diet provided was largely meat and canned vegetables, with almost no fresh food. In the Pennsylvania plant the negroes and whites not only worked in the same departments, but lived in company bunk houses and ate the same food. Both races had about the same standard of cleanliness and both had T.N.T. poisoning. There is, therefore, no indisputable evidence of racial immunity toward T.N.T. as a systemic poison, although negroes are distinctly less liable to T.N.T. dermatitis, as was found in both plants.*

In this respect our experience agrees with that of the French in their munition plants (8). The French employed three races, white, yellow and black, in making and loading dinitrophenol, and at first were impressed with the greater resistance of the Anamites, the yellow race, and the high degree of susceptibility of the white race. Later, however, they discovered that if all conditions were taken into consideration the theory of racial immunity became decidedly questionable. The white men were more intemperate, more uncleanly in their habits, and less obedient to shop rules than were the yellow men, and in addition, the best medical care, which means the most careful examination and diagnosis, was given to the white men. These differences seemed to the French enough to account for the difference in the numbers of cases of D.N.P. poisoning reported from the two groups.

### Influence of Age

Forty per cent. of the employees in the six American plants studied were under 25 years of age, and 22 per cent. under 21 years. The largest proportion of youthful employees — 55 per cent. under 21 years of age — was in Plant 3, fortunately one of the better plants. Miss Hall reported a very marked susceptibility among the younger men under her observation. Only a few men under 25 years were employed in her two plants, but the few that were under that age showed a very low resistance to the poison. Three lads of 19 were dis-

* Marshall, Lynch, Smith, and Williams of the Chemical Warfare Service tested the susceptibility of whites and negroes to mustard gas. A certain degree of resistance was displayed by about 20 to 40 per cent. of the whites, and by 78 per cent. of the negroes. Two per cent. of the whites showed hypersensitivity, but none of the negroes. (G. S. Derby, *Arch. Ophth.*, 1920, **49**, 119.)

charged after three weeks' work, because the doctor was unwilling to take the risk of keeping them longer. One man of 21 years, who was unusually careful and cleanly in his habits, sickened so seriously at the end of the first week that he was discharged. Of all the men who were discharged from the worst of these two factories during one month on account of sickness, one-third were under 25 years of age, while only one-eighth of the entire force employed were under 25.

None of the other students had any such striking incidents to report; indeed, they were not impressed with the oversusceptibility of the younger men, but a close analysis of their records demonstrated it. For instance, forty-eight of TeLinde's cases were divided into two groups, one consisting of twenty-nine lads under 21 years; the other, of nineteen men over 30 years. The period of exposure to T.N.T. before the appearance of the first symptoms of sickness was noted in each case, and it appeared that while the older men had averaged forty-nine days of work before sickening, the younger men averaged only ten and a half days. The young men had for the most part reacted to the T.N.T. with great rapidity, only five out of the twenty-nine working as long as two weeks without feeling any effect. Similar groups from Eversoll's records gave an even greater contrast. The older men averaged fifty-six days' exposure, the younger men only seven to eight days.

Finally, I selected at random from the history sheets of these two plants fifteen records of men who had developed serious symptoms in a very short time, and on referring to the age lists I found that only one of these fifteen was over 21 years of age, and he was only 24 years old. Yet in these two plants the men under 25 years constituted less than 40 per cent. of the force. The early experience with T.N.T. in England showed clearly the greater susceptibility of the young people. The general mortality from toxic jaundice, recognized and notified as such, was 25.9 per cent., but for persons under 18 years of age the proportion was six deaths out of nine cases (3).

### Influence of Sex

The British reports have not shed any light on the question of the influence of sex in T.N.T. poisoning. Although the mortality among the women was greater than among the men — 28.6 per cent. as against 20 per cent. — the women were younger than the men, and the oversusceptibility is attributed by Legge to their youth, not to their sex. We could not come to any conclusion at all with respect to the American cases, since the employees in our plants were almost all men, and the few women employed did relatively safe work. It was possible to obtain records of only thirty-six women employed in four shell-loading and detonator departments. These women were carefully examined, but the results were largely negative. None of them was doing any of the more dangerous work, such as preparing the charge, loading shell or drilling the hole for the detonator charge. Indeed they would have had little or no contact with T.N.T. had they all been employed in well-regulated plants, but sixteen were working in the two plants under Miss Hall's observation where T.N.T. was so recklessly spilled and scattered about that it was impossible to avoid contact with it. Miss Hall examined a group of seven women whose hands were stained from handling shell smeared with T.N.T. Five complained of mild symptoms and three of these gave positive Webster reactions, but none showed cyanosis, and none had applied for treatment, except one married woman who complained of nausea and vomiting, and whom the physician believed to be pregnant. Miss Hall examined another group of nine girls who were pressing

small quantities of dry, pure T.N.T. into detonators. Only one, a girl of 20 years who had worked six weeks longer than any of the others, had fairly serious symptoms. A third group, under TeLinde's observation, working under good conditions and exposed to small quantities of fume and dust had no signs of ill health, although two of the women had Webster reactions of medium intensity. Miss Emery examined ten women who were obliged to come more in contact with amatol than any of the other women, for they were cleaning the outer surface of loaded shell, cleaning the threads of the screw necks, and placing the finished shell in cars. Six of these ten suffered from T.N.T. dermatitis and slight symptoms of systemic poisoning. One of them, a woman of 31 years, seemed unusually susceptible. She had an eruption over her hands, arms and legs, and complained of nausea, loss of appetite, constipation, sore throat and pains in her legs and arms. None of these women was cyanosed.

Summing up, we may say that it was even more impossible to compare the susceptibility of the two sexes to T.N.T. than to compare the susceptibility of negroes and whites, for the exposure of the women and the men was altogether different.

### Effect of Hot and Humid Weather

Every manager and foreman interviewed said that T.N.T. poisoning was more common and severe in hot weather, especially if the humidity was also high. The students in charge of the inquiry, with the exception of Herman and Putnam, worked through the intense heat of August, and all of them reported that the number of cases of sickness increased markedly during the hot days and for a few days just following. Miss Hall wrote that only four men came for treatment during six days when the temperature was between 68° F. and 89° F., but in six days of heat from 90° F. to 106° F. twenty men reported for treatment, and this number did not represent nearly all of the sickness, because on the day of greatest heat the plant was obliged to close down for lack of men and was greatly hampered for two days more.

Curiously enough, heat does not seem to increase T.N.T. dermatitis, contrary to the general impression that prevails among the men. It is true that summer is the season for "T.N.T. itch," but the excessively hot weather of August did not increase the number of cases as it increased the cases of systemic T.N.T. poisoning. There were quite as many cases in cool summer weather as in hot, and the probable explanation for the increase of "itch" in summer is that the men expose more of the skin by rolling up their sleeves and leaving their shirts open at the neck, or by working in low-necked and sleeveless underwear.

### Period of Exposure before Absorption Takes Place

The Webster reaction may appear very early, especially if there is excessive exposure. Miss Hall reported the most striking cases of rapid absorption and elimination of the poison and I have already spoken of the appearance of a positive Webster in her urine after a few hours' sojourn in a badly contaminated department. Miss Hall was able to get reactions of medium intensity in the urines of ten newly employed men at the end of their first six hours of work. Such excessive exposure did not exist in any other plant, but the records of 133 cases in which a maximum Webster reaction was obtained showed that more than a third of the men, 39 per cent., had been exposed no longer than three weeks.

There were plenty of records of men who felt the first symptoms of illness on the first or second day of their employment, but sometimes these symptoms passed away

and the men felt quite well again for a short time; then, after longer exposure, symptoms of another kind developed. TeLinde and Herman and Putnam described in some cases a transitory disturbance of digestion with loss of appetite, a bad taste in the mouth, and usually diarrhea with more or less pain, but no cyanosis or dizziness or headache. The more characteristic symptoms were breathlessness, a feeling of tightness in the chest, headache, dizziness, dullness and lassitude, pains in the limbs, weakness of the knees and lividity of the face with blue lips, and these usually appeared soon after the beginning of T.N.T. work. Even in a well-managed plant the men who were at all susceptible to T.N.T. felt the first symptoms fairly early, nearly a third of them before the first fortnight was over.

It is the general belief of the men who have had experience in T.N.T. work and of some plant physicians that T.N.T. dermatitis is quite distinct from general poisoning and that a man with "the itch" never need fear an attack of serious T.N.T. sickness. The students found several exceptions to this rule. Nine out of twenty-eight patients with dermatitis in the Wisconsin plant had fairly serious general symptoms of poisoning, as did four out of twelve in the Virginia plant. It is clear, however, that an attack of dermatitis may occur from a purely local action of T.N.T. or its impurities, for the majority of the men with dermatitis had negative Webster reactions or very slight reactions.

### Persistence of T.N.T. in the Body

It was, of course, a matter of great practical importance to determine how quickly T.N.T. could be eliminated from the body, and the students were, therefore, instructed to make repeated Webster tests on the urines of men who had been shifted from T.N.T. work or who were in the hospital under treatment. They found that the reaction tended to disappear from the urine within a fortnight after entire removal from T.N.T. work, but that there were instances of delayed elimination quite as striking as the instances of rapid absorption. One of Miss Hall's patients, who was seriously poisoned and gave a Webster 5, was removed from all exposure to T.N.T. but after twelve days it was still possible to get a positive reaction. TeLinde reported a case with positive Webster reaction five weeks after removal from work.

Eversoll and TeLinde were the only students who were able to send full records because the plants under their observation were the only ones in which there was a regular system of shifting men to work free from T.N.T., and keeping them under observation. The most rapid instances of partial and complete disappearance of the Webster reaction came from TeLinde who was able to observe men in the plant hospital where a vigorous eliminative treatment was carried through. The men with T.N.T. sickness were given a thorough scrub bath, a purge, an enema, and a diuretic, and were encouraged to drink large quantities of warm milk. Under this treatment the poison was eliminated fairly rapidly. One boy of 18 years, who had never been sick before, was first examined after he had been exposed to fumes and dust for thirty-five days. He had a Webster 3 at that time. Six days later he came to the hospital with typical symptoms of acute poisoning and a Webster 5. Under the above treatment the reaction fell in thirty-six hours from 5 to 1, and his symptoms had improved greatly, though they had not disappeared. Another man with much the same symptoms, as well as abdominal pain and diarrhea, had a Webster 4 which in twenty-four hours fell to a trace.

Both TeLinde and Eversoll found that a transfer to work free from T.N.T. would re-

sult in a disappearance of the Webster reaction, but much more slowly than under hospital treatment. One of Eversoll's cases was transferred to outdoor work on July 21 because of slight symptoms of poisoning and a Webster 4, but he did not give a negative Webster till August 31. Usually the work to which the man was shifted involved some slight contact with T.N.T., in which case the reaction would persist. An interesting case reported by Eversoll was in a boy of 18 who, because of decided symptoms of poisoning and a maximum Webster, was put on outdoor work every other night. On the morning after such work the reaction would be Webster 1, but on the morning after his shift of pouring T.N.T. it would be Webster 3. A pelleter who had a Webster 4 was transferred to the nitrating department, where there is very little contact with T.N.T. The reaction fell to 3 in six days' time, then gradually to 1, where it persisted. A striking argument in defense of the contention that clean working clothes, clean gloves, and good bathing facilities must be provided for these men was found in the persistence of the Webster reaction in men who continued to wear their dirty gloves after being shifted to T.N.T.-free work. TeLinde had several instances of men with persistent Webster 1 or Webster 2 reactions, even after transference to the empty-shell department, and he came to the conclusion that they were absorbing small quantities of T.N.T. from their soaked gloves.

## Comparative Danger of Crude, Pure and Mixed T.N.T.

In dealing with this question also we were greatly hampered by the varying conditions in the different plants. Miss Hall saw severer cases of poisoning in men loading pure T.N.T. than TeLinde saw in men loading amatol, but in the one case the exposure was excessive, in the other, slight. The negroes in TeLinde's plant certainly showed greater absorption of amatol than of pure T.N.T., those working with amatol giving positive Webster reactions up to 3, while those working with pure T.N.T. gave negative or 2 as the highest reaction. We were not able to say whether more poisoning resulted from crude T.N.T. than from pure T.N.T., or *vice versa*. According to the experiments of Voegtlin and his colleagues (9), there is no difference between crude and purified T.N.T. so far as their effect on animals was observed. The only positive fact that we were able to establish was that crude T.N.T. is more productive of dermatitis than the purified. We had looked for the greatest incidence of eczema and other skin lesions in the dirty, loading plants in the New Jersey meadows, where heat and humidity, excessive exposure, and poor washing facilities would seem to favor it. Instead, it was found that those very plants had the smallest number of cases of T.N.T. itch, and the largest number occurred in the two cool situations, the nitrating plant in northern Wisconsin and the purifying plant in the Pennsylvania mountains. Since the Wisconsin plant was not only the coolest, but was one of the cleanest, had excellent lavatories and employed an unusually high class of labor, it is plain that there must have been something in the material handled that was responsible for the high percentage of dermatitis.

The following figures show the proportion of itch among the men and women in these six plants. It is evident from them that crude T.N.T. is worse than the pure, and that amatol is worse than the unmixed.

| | Percentage of Men with T.N.T. Dermatitis |
|---|---|
| Plants 1 and 2, loading pure T.N.T. | 3.4 |
| Plant 3, loading amatol | 18.0 |
| Plant 4, loading amatol | 20.0 |
| Plant 5, purifying crude T.N.T. | 26.0 |
| Plant 6, manufacturing crude and pure T.N.T. | 31.0 |

### Early Symptoms of T.N.T. Poisoning

Most of the students reported that the first symptom noted by the men was breathlessness on exertion, especially on climbing a hill or going upstairs. A man who said that he had not felt the effect of his work in any way would almost always admit this symptom if he was asked. Next in order came dizziness on stooping over, and more or less persistent headache, or the man complained first of loss of appetite, bad taste in the mouth, and a sensation of nausea in the morning. Sometimes the men who were exposed to dust complained of running of the eyes, smarting and burning in the nose and throat, and nose-bleed. Together with these symptoms, an early case of poisoning is characterized by cramps in the calves of the legs, fatigue disproportionate to the work done, and a feeling of tightness in the chest. Very early in the course of poisoning the man notices a change of color in the urine. It is a clear brown, at first about as dark as weak tea, then increasing till it may be as dark as coffee.

By the time the man feels ill enough to go to the doctor for treatment, he presents a very characteristic appearance. He has an expression of dullness and weariness, heavy eyes, drooping lids, sclerotics slightly yellow, lips and mucous membranes of the mouth blue, the face a leaden or ashen color. In Plant 1, patients with very livid color and lips almost inky were described by Miss Hall.

So far as one can judge from the notes of the students, there did not seem to be two clearly marked varieties of T.N.T. poisoning, the gastric and the cyanotic, such as have been described by some of the English writers. In Plants 3 and 5 a mild gastric form without cyanosis was noted, but these cases cleared up rapidly. No serious gastric case was free from cyanosis, and almost all of the patients with cyanosis, dizziness, faintness, headache and pain in the limbs, showed gastric symptoms also.

When no effort was made by the physician in charge to discover cases of sickness among the men, it sometimes happened that by the time a workman applied for treatment he was already severely poisoned, for apparently serious changes may occur without causing enough suffering to make the man believe that he is really sick. Miss Hall saw a man in the dispensary who had not come to complain of sickness, but of an infected cut. She described him as being strikingly pale, with a grayish yellow color, his lips, ears and tongue deeply cyanosed, and his sclerotics distinctly yellow. He had dyspnea and a pulse of 100. His urine was brownish black and gave a Webster 5, yet on questioning him, she found that he complained of nothing except breathlessness and a slight headache. He was told to return to have the cut dressed every day, but he did not, and when Miss Hall finally discovered his lodging house a week later she was told that he had been sick in bed for four days and had then left for the city. This is a good illustration of the wastefulness caused by poor medical supervision.

The effect of alcohol on T.N.T. poisoning was well known to the workmen in the plants studied. They knew perfectly well that while working with T.N.T. they could not drink without risking serious sickness. Many stories were told of men turning blue in the face and falling unconscious on the floor of a saloon after one or two drinks of whiskey. So notorious was this that the men who wanted to keep on working practically gave up drink, or if they decided to go on a spree they would deliberately lay off work for two or three days before and two or three days after. They described the effect as a sudden, intense flushing of the whole body, with a sensation of heat, a rush of blood to the head, blackness before the eyes, and then loss of consciousness.

Bystanders reported that during the period of complete collapse, the affected man's face was livid and his lips an inky blue.

It was a matter of great surprise to us not to discover a single case of typical toxic jaundice nor of aplastic anemia in any one of these five plants during the time the students were working there. Miss Hall was told that a young girl of 16, who had been working for three months, left on account of sickness and was at that time so deeply jaundiced as to attract attention. She died two weeks later, but it was impossible to trace this case or to secure any information from the physician. It is difficult to explain the absence of toxic jaundice. During 1916, I had found records of thirteen deaths from T.N.T., eleven of them typical toxic jaundice, and there was a much larger number of men employed in 1918 than in 1916. The only explanation that can be given is that in three of these plants medical supervision was careful enough to make it impossible for a case of poisoning to progress to the point of severe jaundice, while in two other plants, all sick men were promptly discharged, and no one knew what happened to them afterward. It must also be remembered that the men were usually exposed to T.N.T. for a very short time only. Out of 374 men, only fifty-seven had worked for more than three months, and British statistics show that toxic jaundice usually does not appear before three months' exposure. In one of the plants, the proportion of those employed as long as three months was only 4 per cent.; in another, 7 per cent.; and in all the labor turnover was very great, decidedly greater than in 1916. Reports did indeed come to me of toxic jaundice and of aplastic anemia in other T.N.T. plants. I had reason to believe that there were twelve or thirteen cases during the last year of the war, but none were in the factories where the students were stationed.

### Significance of the Webster Reaction

The Webster reaction seems to be an admirable test for the absorption of T.N.T., a very rapid and delicate one. The worse the plant is; the larger is the proportion of positive Webster tests. In Plant 1 every urine examined was positive, even if the man had been at work only one day. In Plant 4, which had the best conditions, there were only twenty-one negative reactions out of ninety-eight specimens. As an index of absorption it is certainly valuable. Repeatedly, the intensity of the reaction increased as the days went on. Herman and Putnam applied the tests in about half their cases before and after work, and in about 90 per cent. of these cases the reaction was more intense after an eight-hour shift than before it. The work in this plant was continuous, no holidays or Sundays being observed, but in the others, where the Sunday rest was given, it was repeatedly found that the Webster reaction would be low on Monday and rise gradually to be high on Thursday, Friday and Saturday.

Whether the Webster test is of any other practical value is hard to say. It could not be used as an indication that an acute attack of poisoning was impending, nor was it possible to establish a correspondence between the clinical history and the Webster reaction. While, as a general rule, the intensity of the reaction increased with the increasing severity of an attack, there were too many exceptions to this rule to make it of any practical value. Serious cases sometimes occurred with only a slight Webster reaction, while, on the other hand, a Webster 4 or even a Webster 5 was found in men who had no symptoms of sickness at all. One man with a negative Webster had gastric pain, nausea, vomiting, weakness in the knees, cramps in the calves of the legs, dermatitis on hands, arms and ankles, and general weakness. According to Feldman (10), the Webster reaction, indicating as it

does elimination of T.N.T., should not increase with the onset of severe symptoms, but should diminish or disappear, and Feldman had an opportunity to observe just this phenomenon. The students were asked to bear this possibility in mind and report on it, but Miss Hall was the only one who saw a case with a drop from Webster 3 to 1 as symptoms of poisoning developed. A careful analysis of 137 cases failed to bear out Feldman's theory, for in general the more intense Webster reaction is associated with the more serious form of poisoning.

As a rule Websters 4 and 5 were found among the newly employed, those who had worked less than a month, while the men who had handled T.N.T. for six months and more hardly ever had a reaction of more than 2 or 3, showing that a gradual elimination of the more susceptible men takes place, those that absorb the poison readily dropping out while the relatively immune remain at work.

## Value of Blood and Urine Examinations in the Diagnosis of T.N.T. Poisoning

The examinations made of the blood have been described in detail by Dr. George R. Minot (11), who found a blood picture of enough definiteness and frequency to serve as a valuable guide in the diagnosis of T.N.T. poisoning and in the estimation of the degree of severity of poisoning. As already shown, the Webster reaction cannot give much aid in this respect, but it seems probable that further studies on the urine will bring to light other substances besides the reduction product of T.N.T. which is responsible for the Webster reaction. Certainly it seemed to the students that the changes of color in the untreated urine bore a closer relation to the clinical history of the case than did the varying intensity of the Webster reaction. This color was usually clear light brown to blackish brown and was quite independent of the elimination of T.N.T. as shown by the Webster reaction. Nineteen specimens of dark brown urine, for instance, were either negative to the Webster test or almost negative, while eight which gave a Webster 3 or 4 were normal in color. In one of TeLinde's patients, a man who was shifted from T.N.T. work on account of sickness, the Webster reaction fell from 4 to a trace, while the dark brown color remained unchanged. Two more of his cases dropped to a negative Webster with persistent dark color, while a fourth had a Webster 4 continuously with a normal color. As was to be expected, the darkest specimens came from Plants 1 and 2. Miss Hall reported twenty-five very dark urines, some of them the color of tincture of iodine. She was never able to detect bile in these specimens nor were Putnam and Herman able to do so in theirs.

In some cases the urine changed from a brown to a clear red color, while in others it was red when the first examination was made. These red urines were always associated with a high Webster and with clinical symptoms of poisoning. Among seventy-four specimens, TeLinde found fifteen normal, eight red, and fifty-one brown. Miss Emery found ten normal among forty-seven, nine red, and twenty-eight brown. These observations should, of course, have been supplemented by chemical and microscopic examinations but we did not pursue them further because the Hygienic Laboratory of the Public Health Service had undertaken an intensive study of T.N.T. urines and we did not wish to duplicate their work.

## Summary

The studies made by these students served to emphasize certain practical points in the prevention of T.N.T. poisoning which in all probability apply with

equal force to those nitro and amido derivatives of the benzene ring that are used in the dye and drug industry.

T.N.T. is absorbed chiefly through the skin and, therefore, the most important part of the prevention of T.N.T. sickness is the protection of the worker against direct contact with it. The methods of manufacture, whether or not they necessitate hand work, the cleanliness of the work benches, apparatus, trucks, etc., and the prevention of dust are all of more importance even than the provision of good washing facilities, because a man can wash only at the noon hour and on quitting work, and in the time between these periods he may have his hands and arms continually smeared with T.N.T.

Next in importance to cleanliness of the premises comes the provision of clean working clothes, socks, and gloves. The students' examination showed that T.N.T. could probably be continually absorbed from dirty gloves and dirty overalls. The necessity for providing ample washing facilities, hot and cold running water, soap and towels, and the time to use them, is emphasized, not because it is not perfectly obvious in connection with such a poison as T.N.T., but because it was ignored in several of the T.N.T. plants during the war and is ignored in some of the coal-tar dye works at the present time.

Fumes from melting pots are apparently capable of causing typical T.N.T. poisoning, as is also steam from washing and pelleting, but the more serious forms of T.N.T. sickness are probably never caused by fumes alone.

Hot, humid weather increases general T.N.T. poisoning, but not T.N.T. dermatitis. This last is more prevalent in summer than in winter, but is not increased by very hot weather. Its increase in summer is probably due to the greater exposure of the skin in warm weather.

Young men are more susceptible to T.N.T. than fully grown men. They succumb more quickly and apparently suffer more seriously. It seems poor economy to employ them.

Negroes are not susceptible to T.N.T. dermatitis and may be less susceptible to systemic poisoning than whites, but evidence on this point is not complete.

The application of the Webster test to the urines of approximately 400 T.N.T. workers showed that T.N.T. is rapidly absorbed, but that it can also be rapidly eliminated. Some men could eliminate overnight what had been absorbed during the day; others could get rid of the week's accumulation during Sunday and start on Monday with the urine free from the reduction product. The danger of overtime work and of the seven-day week was shown by these observations and also the value of an occasional vacation of two or three days.

By the use of these same tests it was found that the most economical way to deal with a worker who had absorbed a large amount of T.N.T. was to suspend him altogether from work and subject him to vigorous eliminative treatment. Simply to transfer him to less dangerous work was to postpone his recovery.

No positive aid in the diagnosis of T.N.T. poisoning was found in the Webster reaction in the urine, but the color changes in the untreated urine seemed more significant and worthy of further study. The blood changes found by Dr. Minot are important enough to lead one to hope that careful blood examinations made in workers who are exposed to other benzene derivatives may give similar results, and thus an important aid be gained in the diagnosis of similar forms of industrial poisoning.

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